

CFTRI-MYSORE



4396

Documenta geigy.

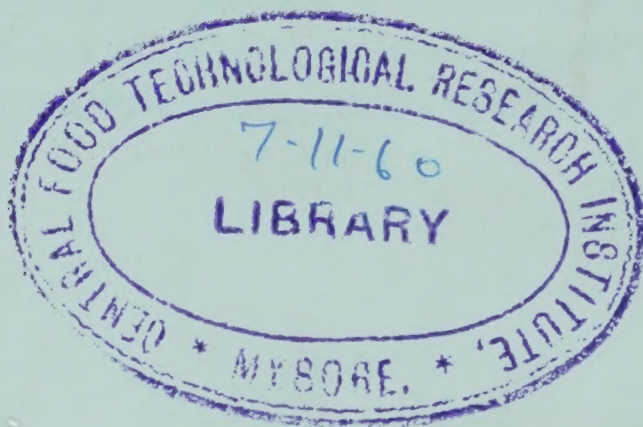
Teng ✓

Documenta Geigy

REFERENCE BOOK
NOT TO BE LENT

Scientific Tables

Fifth Edition (with Supplement)



1959 · Basle (Switzerland) · S. Karger · New York

Postfach
Arnold-Böcklin-Strasse 25

P. O. Box 352
White Plains, N. Y.

REF
4396 (4396) ✓
202

Ae
N59

CFTRI-MYSORE



4396

Documenta geigy...

Foreword

The biological data given in these *Tables* consist of *normal* values unless there is an indication to the contrary. In general, the explanation or definition of all symbols, abbreviations, etc. will be found where these occur. Zero values are indicated throughout by 0. A dash (—) or interrogation mark indicates that the appropriate value is unknown; such indications should on no account be confused with zero values. Data given in brackets are to be regarded as proposed, provisional or unconfirmed. Plus and minus signs (+, —, ++, ——, etc.) are noncommittal indications of indefinite magnitude. Values which are derived from statistical treatment of observational data have been distinguished by printing the mean value in **bold type** and the standard deviation σ in *italics*.

Limitations of space have made it impossible everywhere to include complete bibliographies and as a rule only the principal original papers and reviews have been listed. In the case of subjects in which there is currently great interest more complete bibliographies have been given. The titles of journals have been abbreviated in accordance with the recommendations of the World Health Organization and UNESCO (*World Medical Periodicals*, 1953).

204

Foreword to the Fifth Edition with Supplement

This reprinted Fifth Edition of the Geigy *Scientific Tables* has been produced in response to a widespread demand. The opportunity has been taken not only to correct a number of minor errors but also to include as a Supplement (on pages 427–519) chapters on *Constituents of Living Matter* and *Metabolism* for which we are indebted to Professor Sir Hans KREBS, F.R.S., and co-workers at the University of Oxford. These articles will form part of the revised and enlarged Sixth Edition of the *Scientific Tables* now in preparation.

Contents

Mathematical Tables

Constants	7
Common Logarithms	8
Natural Logarithms	12
Exponential Functions	17
Squares and Square Roots	21
Factorials	24
The Normal Distribution, Areas and Ordinates	25
Probit Transformation	26
Probability	29
<i>t</i> - and χ^2 -Distributions	30
Statistical Methods in Medicine	31

Physical Tables

Units of Measurement	
— Introduction	49
— Symbols and Abbreviations	50
— British and US System, Summary	51
— Weights and Measures	52
— Time and Temperature Units	56
— Mechanical Units	59
— Electrical and Magnetic Units	64
— Units for X-Rays, Gamma Rays and Corpuscular Radiation	70
— Photometric Units	72
— Acoustic Units and Tone Scales	73
— Chemical Units	75
International Biological Standards and Reference Preparations	77
Physical Constants	79

Chemical Tables

The Elements	
— Periodic System	82
— Alphabetical Tables	83
— Properties and Isotopes	84
Application of Artificial Radio-isotopes in Medicine and Biology	98
Molecular Weights of Medically Important Compounds	103
Tenth-Normal Solutions of Reagents	104
Buffer Solutions	105
Indicators, <i>pH</i> Ranges	106
Specific Gravity of Reagent Solutions	107
Hydrometer Scales	109
Aqueous Solutions	
— Introduction	114
— Freezing-point Depression and Osmotic Pressure	116
— Calculation of Salt and Glucose Solutions	117
— Conversion Factors for Electrolytes	118
— Parenteral Infusion Therapy	121
Analytical Conversion Factors	126
Reduction of Gas Volumes to Normal	127

Antibiotics, Pathogenic Organisms, Infectious Diseases

Introduction	128
Characteristics of Pathogenic Organisms, Resulting Diseases, Effects of Antibiotics	129
Systematic Classification of Pathogenic Organisms	169
Index of Pathogenic Organisms and Diseases	172

Hormones

Anterior Pituitary Hormones	179
Posterior Pituitary Hormones	194
Steroid Hormones	195
Adrenaline	205
Insulin	206
Thyroxine	207

Vitamins, Amino-acids, Nutrition

Fat-soluble Vitamins	209
Vitamin C	213
Vitamin B Complex	214
Choline	222

<i>meso</i> Inositol, Vitamin F	223
Essential Amino-acids	224
Daily Requirements of Calories, Proteins, etc.	226
Breast Milk	228
Composition and Calorific Value of Foods	230

Biological and Medical Norms

Basal Metabolism	244
Vital Capacity	251
Height and Weight of Adults	255
Normal Body Measurements during Growth	256
Size and Weight of the Embryo and Infant	267
Appearance of the Secondary Ossification Centres	268
Development of the Teeth	271

Pregnancy and the Puerperium, Semen

Pregnancy	272
Obstetric Norms	275
Semen	276
Spermatozoa	279

Body and Organs, Digestive Secretions, Faeces, Urine

Chemical Composition of the Body and Organs	282
Saliva, Bile, Intestinal and Pancreatic Juices	283
Gastric Juice	284
Faeces	287
Urine	288
Urinary Sediments	292
Routine Tests on Urine	294

Water and Electrolyte Balance

Water Balance	295
Osmotic Relationships	296
Electrolytes	297
Renal Function Values	299

Synopsis of Blood

Circulation Time	301
Blood Pressure	302
Physical Data	303
Coagulation	311
Organic Components	313
Inorganic Components	326
Formed Elements	332
Blood Groups	341

Synopsis of Cerebrospinal Fluid 352

Synopsis of the Eye 355

Posology and Poisoning

Usual and Maximal Doses	367
Posology in Infancy and Childhood	401
Poisoning	422

Supplement

Constituents of Living Matter 427

Metabolism 470

Index to the Supplement 520

General Index 529

Appendices (*leaflets inside back cover*)

Folia Medica GEIGY	
No. 1. The Peripheral Cutaneous Nerves	
No. 2. The Radicular Cutaneous Nerves	
No. 3. Nomogram for Calculation of Body Surface Area	

$$x = 10^{\log x}$$

x is called the number and 10 the base of the logarithm.

The logarithm of a number x to the base 10 is thus the exponent of the power of the base 10 which equals the given number x .

$$\text{Example: } 5 = 10^{\log 5} = 10^{0.6990}; \log 5 = 0.6990$$

Calculation with logarithms to the base 10 is a rewriting of the calculation with powers of the base 10. The following simplifications result:—

multiplications become additions:

$$a \times b = 10^{\log a} \times 10^{\log b} = 10^{\log a + \log b} \quad \left| \quad \log(a \times b) = \log a + \log b \right.$$

divisions become subtractions:

$$a : b = 10^{\log a} : 10^{\log b} = 10^{\log a - \log b} \quad \left| \quad \log(a : b) = \log a - \log b \right.$$

powers become multiplications:

$$a^b = \left(10^{\log a} \right)^b = 10^{(\log a) \times b} \quad \left| \quad \log(a^b) = (\log a) \times b \right.$$

roots become divisions:

$$\sqrt[b]{a} = \sqrt[b]{10^{\log a}} = 10^{(\log a) : b} \quad \left| \quad \log\left(\sqrt[b]{a}\right) = (\log a) : b \right.$$

Calculation with logarithms falls into three parts: Finding the logarithms in the table of logarithms; operating with them according to the above-mentioned rules; return from the resulting logarithm to the number with the aid of the table of antilogarithms.

For the novice the search for the logarithm is best carried out in the following manner: The number for which the logarithm is sought is divided into a factor between one and ten and into a power of ten which, when multiplied by the factor, gives the original number. Simultaneously the factor from one to ten is shortened when necessary to four places after the decimal point for numbers from 1 to 1.0999, and three places after the decimal point for numbers from 1.1 to 9.999. Rounding off is done when necessary.

$$\begin{aligned} \text{Examples:} \quad 10142.8 &\approx 10^4 \times 1.0143 \\ 11370.6 &\approx 10^4 \times 1.137 \\ 0.003436 &= 10^{-3} \times 3.436 \end{aligned}$$

The logarithm of a number can be broken down into an integer called the **characteristic**, and a decimal called the **mantissa**. The characteristic corresponds to the exponent of the power of ten of the number broken down as above, the mantissa is the logarithm of the relevant factor:

$$\begin{aligned} \text{since } 10^4 \times 1.0143 &= 10^{4 + \log 1.0143} \\ \text{then } \log(10^4 \times 1.0143) &= 4 + \log 1.0143 \\ \text{or since } 10^{-3} \times 3.436 &= 10^{-3 + \log 3.436} \\ \text{then } \log(10^{-3} \times 3.436) &= -3 + \log 3.436 \end{aligned}$$

The mantissa is found in the table of logarithms.

$$\text{Example: } \log 1566 = \log(10^3 \times 1.566) = 3 + \log 1.566$$

x	$\log x$	Proportional parts
	6	6
15 1931 17

$$\begin{aligned} \log 1.566 &= 0.1931 \\ &\quad + 17 \\ &= 0.1948 + 3 = \log 1566 = 3.1948 \end{aligned}$$

After the calculation the number corresponding to the resulting logarithm is searched for in the table of antilogarithms in the same way as the logarithms are looked for in the table of logarithms. The characteristic is first put aside, the number corresponding to the mantissa is found and the number of decimal places is then determined by means of the characteristic.

Mathematical Constants

Greek Alphabet

Number*		log ₁₀	Greek character		Greek name	Transcription	
π	3.141 593 (—)	0.4971	Α	α	alpha	Α	a
2 π	6.283 185 (+)	0.7982	Β	β	beta	Β	b
3 π	9.424 778	0.9743	Γ	γ	gamma	Γ	g
π/2	1.570 796 (+)	0.1961	Δ	δ	delta	Δ	d
π/3	1.047 198 (—)	0.0200	Ε	ε	epsilon	Ε	e
π ²	9.869 604 (+)	0.9943	Ζ	ζ	zeta	Ζ	z
π ³	31.006 277 (—)	1.4914	Η	η	eta	Ε̄	ē
√π	1.772 454 (—)	0.2486	Θ	θ	theta	Th	th
√2π	2.506 628 (+)	0.3991	Ι	ι	iota	Ι	i
√π/2	1.253 314 (+)	0.0980	Κ	κ	kappa	Κ	k
∛π	1.464 592 (—)	0.1657	Λ	λ	lambda	Λ	l
e	2.718 282 (—)	0.4343	Μ	μ	mu	Μ	m
e ²	7.389 056	0.8686	Ν	ν	nu	Ν	n
√e	1.648 721 (+)	0.2171	Ξ	ξ	xi	Χ	x
log ₁₀ e**	0.434 294 (+)**	0.6378	Ο	ο	omicron	Ό	ō
log ₁₀ 2/log ₁₀ e = k***	0.693 147 (+)***	0.8408	Π	π	pi	Ρ	p
√2	1.414 214 (—)	0.1505	Ρ	ρ	rho	Ρ	r
√3	1.732 051 (—)	0.2381	Σ	σ	sigma	Σ	s
√10	3.162 278 (—)	0.5000	Τ	τ	tau	Τ	t
∛2	1.259 921	0.1003	Υ	υ	upsilon	Υ	y
∛10	2.154 435 (—)	0.3333	Φ	φ	phi	Ph	ph
			Χ	χ	chi	Ch	ch
			Ψ	ψ	psi	Ps	ps
			Ω	ω	omega	Ό̄	ō̄

* (+) and (—) indicate respectively that the absolute value is greater or less than the approximation given.

** log₁₀ e = M; M × log_e x = log₁₀ x.

*** k/T = λ of the exponential equation N_t = N₀ e^{−λt}; N₀ = amount at arbitrary time zero; N_t = amount at time t; T = half-life measured in the time unit; λ = dN/dt = disintegration constant; t = time measured in the time unit.

Designations and Symbols of Multiples and Submultiples

Symbol	Designation	Factor	
T	Tera-	10 ¹²	1,000,000,000,000
G	Giga-	10 ⁹	1,000,000,000
M	Mega-	10 ⁶	1,000,000
k or K	Kilo-	10 ³	1,000
h	Hecto-	10 ²	100
dk ¹ da ²	Deca-	10 ¹	10
d	Deci-	10 ^{−1}	0.1
c	Centi-	10 ^{−2}	0.01
m	Milli-	10 ^{−3}	0.001
μ	Micro-	10 ^{−6}	0.000001
n	Nano-	10 ^{−9}	0.000000001
p	Pico-	10 ^{−12}	0.000000000001

¹) England and USA. ²) Continental countries.

Logarithmic calculation, see page 6

No. x	$\log x$										Proportional parts								
	0	1	2	3	4	5	6	7	8	9	1	2	3	4	5	6	7	8	9
100	0000	0004	0009	0013	0017	0022	0026	0030	0035	0039	0	1	1	2	2	3	3	3	4
101	0043	0048	0052	0056	0060	0065	0069	0073	0077	0082	0	1	1	2	2	3	3	3	4
102	0086	0090	0095	0099	0103	0107	0111	0116	0120	0124	0	1	1	2	2	3	3	3	4
103	0128	0133	0137	0141	0145	0149	0154	0158	0162	0166	0	1	1	2	2	3	3	3	4
104	0170	0175	0179	0183	0187	0191	0195	0199	0204	0208	0	1	1	2	2	2	3	3	4
105	0212	0216	0220	0224	0228	0233	0237	0241	0245	0249	0	1	1	2	2	2	3	3	4
106	0253	0257	0261	0265	0269	0273	0278	0282	0286	0290	0	1	1	2	2	2	3	3	4
107	0294	0298	0302	0306	0310	0314	0318	0322	0326	0330	0	1	1	2	2	2	3	3	4
108	0334	0338	0342	0346	0350	0354	0358	0362	0366	0370	0	1	1	2	2	2	3	3	4
109	0374	0378	0382	0386	0390	0394	0398	0402	0406	0410	0	1	1	2	2	2	3	3	4
10	0000	0043	0086	0128	0170	0212	0253	0294	0334	0374	4	8	12	17	21	25	29	33	37
11	0414	0453	0492	0531	0569	0607	0645	0682	0719	0755	4	8	11	15	19	23	26	30	34
12	0792	0828	0864	0899	0934	0969	1004	1038	1072	1106	3	7	10	14	17	21	24	28	31
13	1139	1173	1206	1239	1271	1303	1335	1367	1399	1430	3	6	10	13	16	19	23	26	29
14	1461	1492	1523	1553	1584	1614	1644	1673	1703	1732	3	6	9	12	15	18	21	24	27
15	1761	1790	1818	1847	1875	1903	1931	1959	1987	2014	3	6	8	11	14	17	20	22	25
16	2041	2068	2095	2122	2148	2175	2201	2227	2253	2279	3	5	8	11	13	16	18	21	24
17	2304	2330	2355	2380	2405	2430	2455	2480	2504	2529	2	5	7	10	12	15	17	20	22
18	2553	2577	2601	2625	2648	2672	2695	2718	2742	2765	2	5	7	9	12	14	16	19	21
19	2788	2810	2833	2856	2878	2900	2923	2945	2967	2989	2	4	7	9	11	13	16	18	20
20	3010	3032	3054	3075	3096	3118	3139	3160	3181	3201	2	4	6	8	11	13	15	17	19
21	3222	3243	3263	3284	3304	3324	3345	3365	3385	3404	2	4	6	8	10	12	14	16	18
22	3424	3444	3464	3483	3502	3522	3541	3560	3579	3598	2	4	6	8	10	12	14	15	17
23	3617	3636	3655	3674	3692	3711	3729	3747	3766	3784	2	4	6	7	9	11	13	15	17
24	3802	3820	3838	3856	3874	3892	3909	3927	3945	3962	2	4	5	7	9	11	12	14	16
25	3979	3997	4014	4031	4048	4065	4082	4099	4116	4133	2	3	5	7	9	10	12	14	15
26	4150	4166	4183	4200	4216	4232	4249	4265	4281	4298	2	3	5	7	8	10	11	13	15
27	4314	4330	4346	4362	4378	4393	4409	4425	4440	4456	2	3	5	6	8	9	11	13	14
28	4472	4487	4502	4518	4533	4548	4564	4579	4594	4609	2	3	5	6	8	9	11	12	14
29	4624	4639	4654	4669	4683	4698	4713	4728	4742	4757	1	3	4	6	7	9	10	12	13
30	4771	4786	4800	4814	4829	4843	4857	4871	4886	4900	1	3	4	6	7	9	10	11	13
31	4914	4928	4942	4955	4969	4983	4997	5011	5024	5038	1	3	4	6	7	8	10	11	12
32	5051	5065	5079	5092	5105	5119	5132	5145	5159	5172	1	3	4	5	7	8	9	11	12
33	5185	5198	5211	5224	5237	5250	5263	5276	5289	5302	1	3	4	5	6	8	9	10	12
34	5315	5328	5340	5353	5366	5378	5391	5403	5416	5428	1	3	4	5	6	8	9	10	11
35	5441	5453	5465	5478	5490	5502	5514	5527	5539	5551	1	2	4	5	6	7	9	10	11
36	5563	5575	5587	5599	5611	5623	5635	5647	5658	5670	1	2	4	5	6	7	8	10	11
37	5682	5694	5705	5717	5729	5740	5752	5763	5775	5786	1	2	3	5	6	7	8	9	10
38	5798	5809	5821	5832	5843	5855	5866	5877	5888	5899	1	2	3	5	6	7	8	9	10
39	5911	5922	5933	5944	5955	5966	5977	5988	5999	6010	1	2	3	4	5	7	8	9	10
40	6021	6031	6042	6053	6064	6075	6085	6096	6107	6117	1	2	3	4	5	6	8	9	10
41	6128	6138	6149	6160	6170	6180	6191	6201	6212	6222	1	2	3	4	5	6	7	8	9
42	6232	6243	6253	6263	6274	6284	6294	6304	6314	6325	1	2	3	4	5	6	7	8	9
43	6335	6345	6355	6365	6375	6385	6395	6405	6415	6425	1	2	3	4	5	6	7	8	9
44	6435	6444	6454	6464	6474	6484	6493	6503	6513	6522	1	2	3	4	5	6	7	8	9
45	6532	6542	6551	6561	6571	6580	6590	6599	6609	6618	1	2	3	4	5	6	7	8	9
46	6628	6637	6646	6656	6665	6675	6684	6693	6702	6712	1	2	3	4	5	6	7	7	8
47	6721	6730	6739	6749	6758	6767	6776	6785	6794	6803	1	2	3	4	5	5	6	7	8
48	6812	6821	6830	6839	6848	6857	6866	6875	6884	6893	1	2	3	4	5	5	6	7	8
49	6902	6911	6920	6928	6937	6946	6955	6964	6972	6981	1	2	3	4	4	5	6	7	8
x	0	1	2	3	4	5	6	7	8	9	1	2	3	4	5	6	7	8	9

Logarithmic calculation, see page 6

No. <i>x</i>	log <i>x</i>										Proportional parts								
	0	1	2	3	4	5	6	7	8	9	1	2	3	4	5	6	7	8	9
50	6990	6998	7007	7016	7024	7033	7042	7050	7059	7067	1	2	3	3	4	5	6	7	8
51	7076	7084	7093	7101	7110	7118	7126	7135	7143	7152	1	2	3	3	4	5	6	7	8
52	7160	7168	7177	7185	7193	7202	7210	7218	7226	7235	1	2	2	3	4	5	6	7	7
53	7243	7251	7259	7267	7275	7284	7292	7300	7308	7316	1	2	2	3	4	5	6	6	7
54	7324	7332	7340	7348	7356	7364	7372	7380	7388	7396	1	2	2	3	4	5	6	6	7
55	7404	7412	7419	7427	7435	7443	7451	7459	7466	7474	1	2	2	3	4	5	5	6	7
56	7482	7490	7497	7505	7513	7520	7528	7536	7543	7551	1	2	2	3	4	5	5	6	7
57	7559	7566	7574	7582	7589	7597	7604	7612	7619	7627	1	2	2	3	4	5	5	6	7
58	7634	7642	7649	7657	7664	7672	7679	7686	7694	7701	1	1	2	3	4	4	5	6	7
59	7709	7716	7723	7731	7738	7745	7752	7760	7767	✓7774	1	1	2	3	4	4	5	6	7
60	7782	7789	7796	7803	7810	7818	7825	7832	7839	7846	1	1	2	3	4	4	5	6	6
61	7853	7860	7868	7875	7882	7889	7896	7903	7910	7917	1	1	2	3	4	4	5	6	6
62	7924	7931	7938	7945	7952	7959	7966	7973	7980	7987	1	1	2	3	3	4	5	6	6
63	7993	8000	8007	8014	8021	8028	8035	8041	8048	8055	1	1	2	3	3	4	5	5	6
64	8062	8069	8075	8082	8089	8096	8102	8109	8116	8122	1	1	2	3	3	4	5	5	6
65	8129	8136	8142	8149	8156	8162	8169	8176	8182	8189	1	1	2	3	3	4	5	5	6
66	8195	8202	8209	8215	8222	8228	8235	8241	8248	8254	1	1	2	3	3	4	5	5	6
67	8261	8267	8274	8280	8287	8293	8299	8306	8312	8319	1	1	2	3	3	4	5	5	6
68	8325	8331	8338	8344	8351	8357	8363	8370	8376	8382	1	1	2	3	3	4	4	5	6
69	8388	8395	8401	8407	8414	8420	8426	8432	8439	8445	1	1	2	2	3	4	4	5	6
70	8451	8457	8463	8470	8476	8482	8488	8494	8500	8506	1	1	2	2	3	4	4	5	6
71	8513	8519	8525	8531	8537	8543	8549	8555	8561	8567	1	1	2	2	3	4	4	5	5
72	8573	8579	8585	8591	8597	8603	8609	8615	8621	8627	1	1	2	2	3	4	4	5	6
73	8633	8639	8645	8651	8657	8663	8669	8675	8681	8686	1	1	2	2	3	4	4	5	5
74	8692	8698	8704	8710	8716	8722	8727	8733	8739	8745	1	1	2	2	3	4	4	5	5
75	8751	8756	8762	8768	8774	8779	8785	8791	8797	8802	1	1	2	2	3	3	4	5	5
76	8808	8814	8820	8825	8831	8837	8842	8848	8854	8859	1	1	2	2	3	3	4	5	5
77	8865	8871	8876	8882	8887	8893	8899	8904	8910	8915	1	1	2	2	3	3	4	4	5
78	8921	8927	8932	8938	8943	8949	8954	8960	8965	8971	1	1	2	2	3	3	4	4	5
79	8976	8982	8987	8993	8998	9004	9009	9015	9020	9025	1	1	2	2	3	3	4	4	5
80	9031	9036	9042	9047	9053	9058	9063	9069	9074	9079	1	1	2	2	3	3	4	4	5
81	9085	9090	9096	9101	9106	9112	9117	9122	9128	9133	1	1	2	2	3	3	4	4	5
82	9138	9143	9149	9154	9159	9165	9170	9175	9180	9186	1	1	2	2	3	3	4	4	5
83	9191	9196	9201	9206	9212	9217	9222	9227	9232	9238	1	1	2	2	3	3	4	4	5
84	9243	9248	9253	9258	9263	9269	9274	9279	9284	9289	1	1	2	2	3	3	4	4	5
85	9294	9299	9304	9309	9315	9320	9325	9330	9335	9340	1	1	2	2	3	3	4	4	5
86	9345	9350	9355	9360	9365	9370	9375	9380	9385	9390	1	1	2	2	3	3	4	4	5
87	9395	9400	9405	9410	9415	9420	9425	9430	9435	9440	0	1	1	2	2	3	3	4	4
88	9445	9450	9455	9460	9465	9469	9474	9479	9484	9489	0	1	1	2	2	3	3	4	4
89	9494	9499	9504	9509	9513	9518	9523	9528	9533	9538	0	1	1	2	2	3	3	4	4
90	9542	9547	9552	9557	9562	9566	9571	9576	9581	9586	0	1	1	2	2	3	3	4	4
91	9590	9595	9600	9605	9609	9614	9619	9624	9628	9633	0	1	1	2	2	3	3	4	4
92	9638	9643	9647	9652	9657	9661	9666	9671	9675	9680	0	1	1	2	2	3	3	4	4
93	9685	9689	9694	9699	9703	9708	9713	9717	9722	9727	0	1	1	2	2	3	3	4	4
94	9731	9736	9741	9745	9750	9754	9759	9763	9768	9773	0	1	1	2	2	3	3	4	4
95	9777	9782	9786	9791	9795	9800	9805	9809	9814	9818	0	1	1	2	2	3	3	4	4
96	9823	9827	9832	9836	9841	9845	9850	9854	9859	9863	0	1	1	2	2	3	3	4	4
97	9868	9872	9877	9881	9886	9890	9894	9899	9903	9908	0	1	1	2	2	3	3	4	4
98	9912	9917	9921	9926	9930	9934	9939	9943	9948	9952	0	1	1	2	2	3	3	4	4
99	9956	9961	9965	9969	9974	9978	9983	9987	9991	9996	0	1	1	2	2	3	3	3	4
<i>x</i>	0	1	2	3	4	5	6	7	8	9	1	2	3	4	5	6	7	8	9

log x ↗ ↓	x										Proportional parts								
	0	1	2	3	4	5	6	7	8	9	1	2	3	4	5	6	7	8	9
.00	1000	1002	1005	1007	1009	1012	1014	1016	1019	1021	0	0	1	1	1	1	2	2	2
.01	1023	1026	1028	1030	1033	1035	1038	1040	1042	1045	0	0	1	1	1	1	2	2	2
.02	1047	1050	1052	1054	1057	1059	1062	1064	1067	1069	0	0	1	1	1	1	2	2	2
.03	1072	1074	1076	1079	1081	1084	1086	1089	1091	1094	0	0	1	1	1	1	2	2	2
.04	1096	1099	1102	1104	1107	1109	1112	1114	1117	1119	0	1	1	1	1	2	2	2	2
.05	1122	1125	1127	1130	1132	1135	1138	1140	1143	1146	0	1	1	1	1	2	2	2	2
.06	1148	1151	1153	1156	1159	1161	1164	1167	1169	1172	0	1	1	1	1	2	2	2	2
.07	1175	1178	1180	1183	1186	1189	1191	1194	1197	1199	0	1	1	1	1	2	2	2	2
.08	1202	1205	1208	1211	1213	1216	1219	1222	1225	1227	0	1	1	1	1	2	2	2	3
.09	1230	1233	1236	1239	1242	1245	1247	1250	1253	1256	0	1	1	1	1	2	2	2	3
.10	1259	1262	1265	1268	1271	1274	1276	1279	1282	1285	0	1	1	1	1	2	2	2	3
.11	1288	1291	1294	1297	1300	1303	1306	1309	1312	1315	0	1	1	1	2	2	2	3	3
.12	1318	1321	1324	1327	1330	1334	1337	1340	1343	1346	0	1	1	1	2	2	2	2	3
.13	1349	1352	1355	1358	1361	1365	1368	1371	1374	1377	0	1	1	1	2	2	2	3	3
.14	1380	1384	1387	1390	1393	1396	1400	1403	1406	1409	0	1	1	1	2	2	2	3	3
.15	1413	1416	1419	1422	1426	1429	1432	1435	1439	1442	0	1	1	1	2	2	2	3	3
.16	1445	1449	1452	1455	1459	1462	1466	1469	1472	1476	0	1	1	1	2	2	2	3	3
.17	1479	1483	1486	1489	1493	1496	1500	1503	1507	1510	0	1	1	1	2	2	2	3	3
.18	1514	1517	1521	1524	1528	1531	1535	1538	1542	1545	0	1	1	1	2	2	2	3	3
.19	1549	1552	1556	1560	1563	1567	1570	1574	1578	1581	0	1	1	1	2	2	3	3	3
.20	1585	1589	1592	1596	1600	1603	1607	1611	1614	1618	0	1	1	1	2	2	3	3	3
.21	1622	1626	1629	1633	1637	1641	1644	1648	1652	1656	0	1	1	1	2	2	3	3	3
.22	1660	1663	1667	1671	1675	1679	1683	1687	1690	1694	0	1	1	1	2	2	3	3	3
.23	1698	1702	1706	1710	1714	1718	1722	1726	1730	1734	0	1	1	1	2	2	3	3	4
.24	1738	1742	1746	1750	1754	1758	1762	1766	1770	1774	0	1	1	1	2	2	3	3	4
.25	1778	1782	1786	1791	1795	1799	1803	1807	1811	1816	0	1	1	1	2	2	3	3	4
.26	1820	1824	1828	1832	1837	1841	1845	1849	1854	1858	0	1	1	1	2	2	3	3	4
.27	1862	1866	1871	1875	1879	1884	1888	1892	1897	1901	0	1	1	1	2	2	3	3	4
.28	1905	1910	1914	1919	1923	1928	1932	1936	1941	1945	0	1	1	1	2	2	3	4	4
.29	1950	1954	1959	1963	1968	1972	1977	1982	1986	1991	0	1	1	1	2	2	3	4	4
.30	1995	2000	2004	2009	2014	2018	2023	2028	2032	2037	0	1	1	1	2	2	3	4	4
.31	2042	2046	2051	2056	2061	2065	2070	2075	2080	2084	0	1	1	1	2	2	3	4	4
.32	2089	2094	2099	2104	2109	2113	2118	2123	2128	2133	0	1	1	1	2	2	3	4	4
.33	2138	2143	2148	2153	2158	2163	2168	2173	2178	2183	0	1	1	1	2	2	3	4	4
.34	2188	2193	2198	2203	2208	2213	2218	2223	2228	2234	1	1	2	2	3	3	4	4	5
.35	2239	2244	2249	2254	2259	2265	2270	2275	2280	2286	1	1	2	2	3	3	4	4	5
.36	2291	2296	2301	2307	2312	2317	2323	2328	2333	2339	1	1	2	2	3	3	4	4	5
.37	2344	2350	2355	2360	2366	2371	2377	2382	2388	2393	1	1	2	2	3	3	4	4	5
.38	2399	2404	2410	2415	2421	2427	2432	2438	2443	2449	1	1	2	2	3	3	4	4	5
.39	2455	2460	2466	2472	2477	2483	2489	2495	2500	2506	1	1	2	2	3	3	4	5	5
.40	2512	2518	2523	2529	2535	2541	2547	2553	2559	2564	1	1	2	2	3	4	4	5	5
.41	2570	2576	2582	2588	2594	2600	2606	2612	2618	2624	1	1	2	2	3	4	4	5	5
.42	2630	2636	2642	2649	2655	2661	2667	2673	2679	2685	1	1	2	2	3	4	4	5	6
.43	2692	2698	2704	2710	2716	2723	2729	2735	2742	2748	1	1	2	3	3	4	4	5	6
.44	2754	2761	2767	2773	2780	2786	2793	2799	2805	2812	1	1	2	3	3	4	4	5	6
.45	2818	2825	2831	2838	2844	2851	2858	2864	2871	2877	1	1	2	3	3	4	5	5	6
.46	2884	2891	2897	2904	2911	2917	2924	2931	2938	2944	1	1	2	3	3	4	5	5	6
.47	2951	2958	2965	2972	2979	2985	2992	2999	3006	3013	1	1	2	3	3	4	5	5	6
.48	3020	3027	3034	3041	3048	3055	3062	3069	3076	3083	1	1	2	3	4	4	5	6	6
.49	3090	3097	3105	3112	3119	3126	3133	3141	3148	3155	1	1	2	3	4	4	5	6	6
x	0	1	2	3	4	5	6	7	8	9	1	2	3	4	5	6	7	8	9

Logarithmic calculation, see page 6

log x	x										Proportional parts								
	0	1	2	3	4	5	6	7	8	9	1	2	3	4	5	6	7	8	9
<div><div>→</div><div>↓</div></div>																			
.50	3162	3170	3177	3184	3192	3199	3206	3214	3221	3228	1	1	2	3	4	4	5	6	7
.51	3236	3243	3251	3258	3266	3273	3281	3289	3296	3304	1	2	2	3	4	5	5	6	7
.52	3311	3319	3327	3334	3342	3350	3357	3365	3373	3381	1	2	2	3	4	5	5	6	7
.53	3388	3396	3404	3412	3420	3428	3436	3443	3451	3459	1	2	2	3	4	5	6	6	7
.54	3467	3475	3483	3491	3499	3508	3516	3524	3532	3540	1	2	2	3	4	5	6	6	7
.55	3548	3556	3565	3573	3581	3589	3597	3606	3614	3622	1	2	2	3	4	5	6	7	7
.56	3631	3639	3648	3656	3664	3673	3681	3690	3698	3707	1	2	3	3	4	5	6	7	8
.57	3715	3724	3733	3741	3750	3758	3767	3776	3784	3793	1	2	3	3	4	5	6	7	8
.58	3802	3811	3819	3828	3837	3846	3855	3864	3873	3882	1	2	3	4	4	5	6	7	8
.59	3890	3899	3908	3917	3926	3936	3945	3954	3963	3972	1	2	3	4	5	5	6	7	8
.60	3981	3990	3999	4009	4018	4027	4036	4046	4055	4064	1	2	3	4	5	6	6	7	8
.61	4074	4083	4093	4102	4111	4121	4130	4140	4150	4159	1	2	3	4	5	6	7	8	9
.62	4169	4178	4188	4198	4207	4217	4227	4236	4246	4256	1	2	3	4	5	6	7	8	9
.63	4266	4276	4285	4295	4305	4315	4325	4335	4345	4355	1	2	3	4	5	6	7	8	9
.64	4365	4375	4385	4395	4406	4416	4426	4436	4446	4457	1	2	3	4	5	6	7	8	9
.65	4467	4477	4487	4498	4508	4519	4529	4539	4550	4560	1	2	3	4	5	6	7	8	9
.66	4571	4581	4592	4603	4613	4624	4634	4645	4656	4667	1	2	3	4	5	6	7	9	10
.67	4677	4688	4699	4710	4721	4732	4742	4753	4764	4775	1	2	3	4	5	7	8	9	10
.68	4786	4797	4808	4819	4831	4842	4853	4864	4875	4887	1	2	3	4	6	7	8	9	10
.69	4898	4909	4920	4932	4943	4955	4966	4977	4989	5000	1	2	3	5	6	7	8	9	10
.70	5012	5023	5035	5047	5058	5070	5082	5093	5105	5117	1	2	4	5	6	7	8	9	11
.71	5129	5140	5152	5164	5176	5188	5200	5212	5224	5236	1	2	4	5	6	7	8	10	11
.72	5248	5260	5272	5284	5297	5309	5321	5333	5346	5358	1	2	4	5	6	7	9	10	11
.73	5370	5383	5395	5408	5420	5433	5445	5458	5470	5483	1	3	4	5	6	8	9	10	11
.74	5495	5508	5521	5534	5546	5559	5572	5585	5598	5610	1	3	4	5	6	8	9	10	12
.75	5623	5636	5649	5662	5675	5689	5702	5715	5728	5741	1	3	4	5	7	8	9	10	12
.76	5754	5768	5781	5794	5808	5821	5834	5848	5861	5875	1	3	4	5	7	8	9	11	12
.77	5888	5902	5916	5929	5943	5957	5970	5984	5998	6012	1	3	4	5	7	8	10	11	12
.78	6026	6039	6053	6067	6081	6095	6109	6124	6138	6152	1	3	4	6	7	8	10	11	13
.79	6166	6180	6194	6209	6223	6237	6252	6266	6281	6295	1	3	4	6	7	9	10	11	13
.80	6310	6324	6339	6353	6368	6383	6397	6412	6427	6442	1	3	4	6	7	9	10	12	13
.81	6457	6471	6486	6501	6516	6531	6546	6561	6577	6592	2	3	5	6	8	9	11	12	14
.82	6607	6622	6637	6653	6668	6683	6699	6714	6730	6745	2	3	5	6	8	9	11	12	14
.83	6761	6776	6792	6808	6823	6839	6855	6871	6887	6902	2	3	5	6	8	9	11	13	14
.84	6918	6934	6950	6966	6982	6998	7015	7031	7047	7063	2	3	5	6	8	10	11	13	15
.85	7079	7096	7112	7129	7145	7161	7178	7194	7211	7228	2	3	5	7	8	10	12	13	15
.86	7244	7261	7278	7295	7311	7328	7345	7362	7379	7396	2	3	5	7	8	10	12	13	15
.87	7413	7430	7447	7464	7482	7499	7516	7534	7551	7568	2	3	5	7	9	10	12	14	16
.88	7586	7603	7621	7638	7656	7674	7691	7709	7727	7745	2	4	5	7	9	11	12	14	16
.89	7762	7780	7798	7816	7834	7852	7870	7889	7907	7925	2	4	5	7	9	11	13	14	16
.90	7943	7962	7980	7998	8017	8035	8054	8072	8091	8110	2	4	6	7	9	11	13	15	17
.91	8128	8147	8166	8185	8204	8222	8241	8260	8279	8299	2	4	6	8	9	11	13	15	17
.92	8318	8337	8356	8375	8395	8414	8433	8453	8472	8492	2	4	6	8	10	12	14	15	17
.93	8511	8531	8551	8570	8590	8610	8630	8650	8670	8690	2	4	6	8	10	12	14	16	18
.94	8710	8730	8750	8770	8790	8810	8831	8851	8872	8892	2	4	6	8	10	12	14	16	18
.95	8913	8933	8954	8974	8995	9016	9036	9057	9078	9099	2	4	6	8	10	12	15	17	19
.96	9120	9141	9162	9183	9204	9226	9247	9268	9290	9311	2	4	6	8	11	13	15	17	19
.97	9333	9354	9376	9397	9419	9441	9462	9484	9506	9528	2	4	7	9	11	13	15	17	20
.98	9550	9572	9594	9616	9638	9661	9683	9705	9727	9750	2	4	7	9	11	13	16	18	20
.99	9772	9795	9817	9840	9863	9886	9908	9931	9954	9977	2	5	7	9	11	14	16	18	20
x	0	1	2	3	4	5	6	7	8	9	1	2	3	4	5	6	7	8	9

N	0	1	2	3	4	5	6	7	8	9
0.00	— ∞	—6.90776	—6.21461	—5.80914	—5.52146	—5.29832	—5.11600	—4.96185	—4.82831	—4.71053
.01	—4.60517	—4.50986	—4.42285	—4.34281	—4.26870	—4.19971	—4.13517	—4.07454	—4.01738	—3.96332
.02	—3.91202	—3.86323	—3.81671	—3.77226	—3.72970	—3.68888	—3.64966	—3.61192	—3.57555	—3.54046
.03	.50656	.47377	.44202	.41125	.38139	.35241	.32424	.29684	.27017	.24419
.04	.21888	.19418	.17009	.14656	.12357	.10109	.07911	.05761	.03655	.01593
.05	—2.99573	—2.97593	—2.95651	—2.93746	—2.91877	—2.90042	—2.88240	—2.86470	—2.84731	—2.83022
.06	.81341	.79688	.78062	.76462	.74887	.73337	.71810	.70306	.68825	.67365
.07	.65926	.64508	.63109	.61730	.60369	.59027	.57702	.56395	.55105	.53831
.08	.52573	.51331	.50104	.48891	.47694	.46510	.45341	.44185	.43042	.41912
.09	.40795	.39690	.38597	.37516	.36446	.35388	.34341	.33304	.32279	.31264
0.10	—2.30259	—2.29263	—2.28278	—2.27303	—2.26336	—2.25379	—2.24432	—2.23493	—2.22562	—2.21641
.11	.20727	.19823	.18926	.18037	.17156	.16282	.15417	.14558	.13707	.12863
.12	.12026	.11196	.10373	.09557	.08747	.07944	.07147	.06357	.05573	.04794
.13	.04022	.03256	.02495	.01741	.00992	.00248	—1.99510	—1.98777	—1.98050	—1.97328
.14	—1.96611	—1.95900	—1.95193	—1.94491	—1.93794	—1.93102	.92415	.91732	.91054	.90381
.15	—1.89712	—1.89048	—1.88387	—1.87732	—1.87080	—1.86433	—1.85790	—1.85151	—1.84516	—1.83885
.16	.83258	.82635	.82016	.81401	.80789	.80181	.79577	.78976	.78379	.77786
.17	.77196	.76609	.76026	.75446	.74870	.74297	.73727	.73161	.72597	.72037
.18	.71480	.70926	.70375	.69827	.69282	.68740	.68201	.67665	.67131	.66601
.19	.66073	.65548	.65026	.64507	.63990	.63476	.62964	.62455	.61949	.61445
0.20	—1.60944	—1.60445	—1.59949	—1.59455	—1.58964	—1.58475	—1.57988	—1.57504	—1.57022	—1.56542
.21	.56065	.55590	.55117	.54646	.54178	.53712	.53248	.52786	.52326	.51868
.22	.51413	.50959	.50508	.50058	.49611	.49165	.48722	.48281	.47841	.47403
.23	.46968	.46534	.46102	.45672	.45243	.44817	.44392	.43970	.43548	.43129
.24	.42712	.42296	.41882	.41469	.41059	.40650	.40242	.39837	.39433	.39030
.25	—1.38629	—1.38230	—1.37833	—1.37437	—1.37042	—1.36649	—1.36258	—1.35868	—1.35480	—1.35093
.26	.34707	.34323	.33941	.33560	.33181	.32803	.32426	.32051	.31677	.31304
.27	.30933	.30564	.30195	.29828	.29463	.29098	.28735	.28374	.28013	.27654
.28	.27297	.26940	.26585	.26231	.25878	.25527	.25176	.24827	.24479	.24133
.29	.23787	.23443	.23100	.22758	.22418	.22078	.21740	.21402	.21066	.20731
0.30	—1.20397	—1.20065	—1.19733	—1.19402	—1.19073	—1.18744	—1.18417	—1.18091	—1.17766	—1.17441
.31	.17118	.16796	.16475	.16155	.15836	.15518	.15201	.14885	.14570	.14256
.32	.13943	.13631	.13320	.13010	.12701	.12393	.12086	.11780	.11474	.11170
.33	.10866	.10564	.10262	.09961	.09661	.09362	.09064	.08767	.08471	.08176
.34	.07881	.07587	.07294	.07002	.06711	.06421	.06132	.05843	.05555	.05268
.35	—1.04982	—1.04697	—1.04412	—1.04129	—1.03846	—1.03564	—1.03282	—1.03002	—1.02722	—1.02443
.36	.02165	.01888	.01611	.01335	.01060	.00786	.00512	.00239	—0.99967	—0.99696
.37	—0.99425	—0.99155	—0.98886	—0.98618	—0.98350	—0.98083	—0.97817	—0.97551	.97286	.97022
.38	.96758	.96496	.96233	.95972	.95711	.95451	.95192	.94933	.94675	.94418
.39	.94161	.93905	.93649	.93395	.93140	.92887	.92634	.92382	.92130	.91879
0.40	—0.91629	—0.91379	—0.91130	—0.90882	—0.90634	—0.90387	—0.90140	—0.89894	—0.89649	—0.89404
.41	.89160	.88916	.88673	.88431	.88189	.87948	.87707	.87467	.87227	.86988
.42	.86750	.86512	.86275	.86038	.85802	.85567	.85332	.85097	.84863	.84630
.43	.84397	.84165	.83933	.83702	.83471	.83241	.83011	.82782	.82554	.82326
.44	.82098	.81871	.81645	.81419	.81193	.80968	.80744	.80520	.80296	.80073
.45	—0.79851	—0.79629	—0.79407	—0.79186	—0.78966	—0.78746	—0.78526	—0.78307	—0.78089	—0.77871
.46	.77653	.77436	.77219	.77003	.76787	.76572	.76357	.76143	.75929	.75715
.47	.75502	.75290	.75078	.74866	.74655	.74444	.74234	.74024	.73814	.73605
.48	.73397	.73189	.72981	.72774	.72567	.72361	.72155	.71949	.71744	.71539
.49	.71335	.71131	.70928	.70725	.70522	.70320	.70118	.69917	.69716	.69515
0.50	—0.69315	—0.69115	—0.68916	—0.68717	—0.68518	—0.68320	—0.68122	—0.67924	—0.67727	—0.67531
.51	.67334	.67139	.66943	.66748	.66553	.66359	.66165	.65971	.65778	.65585
.52	.65393	.65201	.65009	.64817	.64626	.64436	.64245	.64055	.63866	.63677
.53	.63488	.63299	.63111	.62923	.62736	.62549	.62362	.62176	.61990	.61804
.54	.61619	.61434	.61249	.61065	.60881	.60697	.60514	.60331	.60148	.59966
.55	—0.59784	—0.59602	—0.59421	—0.59240	—0.59059	—0.58879	—0.58699	—0.58519	—0.58340	—0.58161
.56	.57982	.57803	.57625	.57448	.57270	.57093	.56916	.56740	.56563	.56387
.57	.56212	.56037	.55862	.55687	.55513	.55339	.55165	.54991	.54818	.54645
.58	.54473	.54300	.54128	.53957	.53785	.53614	.53444	.53273	.53103	.52933
.59	.52763	.52594	.52425	.52256	.52088	.51919	.51751	.51584	.51416	.51249
0.60	—0.51083	—0.50916	—0.50750	—0.50584	—0.50418	—0.50253	—0.50088	—0.49923	—0.49758	—0.49594
.61	.49430	.49266	.49102	.48939	.48776	.48613	.48451	.48289	.48127	.47965
.62	.47804	.47642	.47482	.47321	.47160	.47000	.46840	.46681	.46522	.46362
.63	.46204	.46045	.45887	.45728	.45571	.45413	.45256	.45099	.44942	.44785
.64	.44629	.44473	.44317	.44161	.44006	.43850	.43696	.43541	.43386	.43232
.65	—0.43078	—0.42925	—0.42771	—0.42618	—0.42465	—0.42312	—0.42159	—0.42007	—0.41855	—0.41703
.66	.41552	.41400	.41249	.41098	.40947	.40797	.40647	.40497	.40347	.40197
.67	.40048	.39899	.39750	.39601	.39453	.39304	.39156	.39008	.38861	.38713
.68	.38566	.38419	.38273	.38126	.37980	.37834	.37688	.37542	.37397	.37251
.69	.37106	.36962	.36817	.36673	.36528	.36384	.36241	.36097	.35954	.35810
0.70	—0.35667	—0.35525	—0.35382	—0.35240	—0.35098	—0.34956	—0.34814	—0.34672	—0.34531	—0.34390
.71	.34249	.34108	.33968	.33827	.33687	.33547	.33408	.33268	.33129	.32989
.72	.32850	.32712	.32573	.32435	.32296	.32158	.32021	.31883	.31745	.31608
.73	.31471	.31334	.31197	.31061	.30925	.30788	.30653	.30517	.30381	.30246
.74	.30111	.29975	.29841	.29706	.29571	.29437	.29303	.29169	.29035	.28902
.75	—0.28768	—0.28635	—0.28502	—0.28369	—0.28236	—0.28104	—0.27971	—0.27839	—0.27707	—0.27575
.76	.27444	.27312	.27181	.27050	.26919	.26788	.26657	.26527	.26397	.26266
.77	.26136	.26007	.25877	.25748	.25618	.25489	.25360	.25231	.25103	.24974
.78	.24846	.24718	.24590	.24462	.24335	.24207	.24080	.23953	.23826	.23699
.79	.23572	.23446	.23319	.23193	.23067	.22941	.22816	.22690	.22565	.22439

¹) To find the natural logarithm (\log_e) of a number which is a power of ten less or greater than a number given in the Tables: if the number concerned is less, e.g. $\frac{1}{10}$ (10^{-1}), $\frac{1}{100}$ (10^{-2}), $\frac{1}{1000}$ (10^{-3}), etc. *subtract* from the given logarithm $\log_e 10$, $2 \log_e 10$, $3 \log_e 10$, etc.; if the number concerned is greater, e.g. 10 times (10^1), 100 times (10^2), 1000 times (10^3), etc. *add* to the given logarithm $\log_e 10$, $2 \log_e 10$, $3 \log_e 10$, etc.
Example: $\log_e 0.02 = \log_e 0.2 - \log_e 10$ or $\log_e 2000 = \log_e 200 + \log_e 10$.

N	0	1	2	3	4	5	6	7	8	9
0.80	—0.22314	—0.22189	—0.22065	—0.21940	—0.21816	—0.21691	—0.21567	—0.21443	—0.21319	—0.21196
.81	.21072	.20949	.20825	.20702	.20579	.20457	.20334	.20212	.20089	.19967
.82	.19845	.19723	.19601	.19480	.19358	.19237	.19116	.18995	.18874	.18754
.83	.18633	.18513	.18392	.18272	.18152	.18032	.17913	.17793	.17674	.17554
.84	.17435	.17316	.17198	.17079	.16960	.16842	.16724	.16605	.16487	.16370
.85	—0.16252	—0.16134	—0.16017	—0.15900	—0.15782	—0.15665	—0.15548	—0.15432	—0.15315	—0.15199
.86	.15032	.14966	.14850	.14734	.14618	.14503	.14387	.14272	.14156	.14041
.87	.13926	.13811	.13697	.13582	.13467	.13353	.13239	.13125	.13011	.12897
.88	.12783	.12670	.12556	.12443	.12330	.12217	.12104	.11991	.11878	.11766
.89	.11653	.11541	.11429	.11317	.11205	.11093	.10981	.10870	.10759	.10647
0.90	—0.10536	—0.10425	—0.10314	—0.10203	—0.10093	—0.09982	—0.09872	—0.09761	—0.09651	—0.09541
.91	.09431	.09321	.09212	.09102	.08992	.08883	.08774	.08665	.08556	.08447
.92	.08338	.08230	.08121	.08013	.07904	.07796	.07688	.07580	.07472	.07365
.93	.07257	.07150	.07042	.06935	.06828	.06721	.06614	.06507	.06401	.06294
.94	.06188	.06081	.05975	.05869	.05763	.05657	.05551	.05446	.05340	.05235
.95	—0.05129	—0.05024	—0.04919	—0.04814	—0.04709	—0.04604	—0.04500	—0.04395	—0.04291	—0.04186
.96	.04082	.03978	.03874	.03770	.03666	.03563	.03459	.03356	.03252	.03149
.97	.03046	.02943	.02840	.02737	.02634	.02532	.02429	.02327	.02225	.02122
.98	.02020	.01918	.01816	.01715	.01613	.01511	.01410	.01309	.01207	.01106
.99	.01005	.00904	.00803	.00702	.00602	.00501	.00401	.00300	.00200	.00100

1.00—6.49

1.0	0.00000	0.00995	0.01980	0.02956	0.03922	0.04879	0.05827	0.06766	0.07696	0.08618
.1	.09531	.10436	.11333	.12222	.13103	.13976	.14842	.15700	.16551	.17395
.2	.18232	.19062	.19885	.20701	.21511	.22314	.23111	.23902	.24686	.25464
.3	.26236	.27003	.27763	.28518	.29267	.30010	.30748	.31481	.32208	.32930
.4	.33647	.34359	.35066	.35767	.36464	.37156	.37844	.38526	.39204	.39878
.5	0.40547	0.41211	0.41871	0.42527	0.43178	0.43825	0.44469	0.45108	0.45742	0.46373
.6	.47000	.47623	.48243	.48858	.49470	.50078	.50682	.51282	.51879	.52473
.7	.53063	.53649	.54232	.54812	.55389	.55962	.56531	.57098	.57661	.58222
.8	.58779	.59333	.59884	.60432	.60977	.61519	.62058	.62594	.63127	.63658
.9	.64185	.64710	.65233	.65752	.66269	.66783	.67294	.67803	.68310	.68813
2.0	0.69315	0.69813	0.70310	0.70804	0.71295	0.71784	0.72271	0.72755	0.73237	0.73716
.1	.74194	.74669	.75142	.75612	.76081	.76547	.77011	.77473	.77932	.78390
.2	.78846	.79299	.79751	.80200	.80648	.81093	.81536	.81978	.82418	.82855
.3	.83291	.83725	.84157	.84587	.85015	.85442	.85866	.86289	.86710	.87129
.4	.87547	.87963	.88377	.88789	.89200	.89609	.90016	.90422	.90826	.91228
.5	0.91629	0.92028	0.92426	0.92822	0.93216	0.93609	0.94001	0.94391	0.94779	0.95166
.6	.95551	.95935	.96317	.96698	.97078	.97456	.97833	.98208	.98582	.98954
.7	.99325	.99695	1.00063	1.00430	1.00796	1.01160	1.01523	1.01885	1.02245	1.02604
.8	1.02962	1.03318	.03674	.04028	.04380	.04732	.05082	.05431	.05779	.06126
.9	.06471	.06815	.07158	.07500	.07841	.08181	.08519	.08856	.09192	.09527
3.0	1.09861	1.10194	1.10526	1.10856	1.11186	1.11514	1.11841	1.12168	1.12493	1.12817
.1	.13140	.13462	.13783	.14103	.14422	.14740	.15057	.15373	.15688	.16002
.2	.16315	.16627	.16938	.17248	.17557	.17865	.18173	.18479	.18784	.19089
.3	.19392	.19695	.19996	.20297	.20597	.20896	.21194	.21491	.21788	.22083
.4	.22378	.22671	.22964	.23256	.23547	.23837	.24127	.24415	.24703	.24990
.5	1.25276	1.25562	1.25846	1.26130	1.26413	1.26695	1.26976	1.27257	1.27536	1.27815
.6	.28093	.28371	.28647	.28923	.29198	.29473	.29746	.30019	.30291	.30563
.7	.30833	.31103	.31372	.31641	.31909	.32176	.32442	.32708	.32972	.33237
.8	.33500	.33763	.34025	.34286	.34547	.34807	.35067	.35325	.35584	.35841
.9	.36098	.36354	.36609	.36864	.37118	.37372	.37624	.37877	.38128	.38379
4.0	1.38629	1.38879	1.39128	1.39377	1.39624	1.39872	1.40118	1.40364	1.40610	1.40854
.1	.41099	.41342	.41585	.41828	.42070	.42311	.42552	.42792	.43031	.43270
.2	.43508	.43746	.43984	.44220	.44456	.44692	.44927	.45161	.45395	.45629
.3	.45862	.46094	.46326	.46557	.46787	.47018	.47247	.47476	.47705	.47933
.4	.48160	.48387	.48614	.48840	.49065	.49290	.49515	.49739	.49962	.50185
.5	1.50408	1.50630	1.50851	1.51072	1.51293	1.51513	1.51732	1.51951	1.52170	1.52388
.6	.52606	.52823	.53039	.53256	.53471	.53687	.53902	.54116	.54330	.54543
.7	.54756	.54969	.55181	.55393	.55604	.55814	.56025	.56235	.56444	.56653
.8	.56862	.57070	.57277	.57485	.57691	.57898	.58104	.58309	.58515	.58719
.9	.58924	.59127	.59331	.59534	.59737	.59939	.60141	.60342	.60543	.60744
5.0	1.60944	1.61144	1.61343	1.61542	1.61741	1.61939	1.62137	1.62334	1.62531	1.62728
.1	.62924	.63120	.63315	.63511	.63705	.63900	.64094	.64287	.64481	.64673
.2	.64866	.65058	.65250	.65441	.65632	.65823	.66013	.66203	.66393	.66582
.3	.66771	.66959	.67147	.67335	.67523	.67710	.67896	.68083	.68269	.68455
.4	.68640	.68825	.69010	.69194	.69378	.69562	.69745	.69928	.70111	.70293
.5	1.70475	1.70656	1.70838	1.71019	1.71199	1.71380	1.71560	1.71740	1.71919	1.72098
.6	.72277	.72455	.72633	.72811	.72988	.73166	.73342	.73519	.73695	.73871
.7	.74047	.74222	.74397	.74572	.74746	.74920	.75094	.75267	.75440	.75613
.8	.75786	.75958	.76130	.76302	.76473	.76644	.76815	.76985	.77156	.77326
.9	.77495	.77665	.77834	.78002	.78171	.78339	.78507	.78675	.78842	.79009
6.0	1.79176	1.79342	1.79509	1.79675	1.79840	1.80006	1.80171	1.80336	1.80500	1.80665
.1	.80829	.80993	.81156	.81319	.81482	.81645	.81808	.81970	.82132	.82294
.2	.82455	.82616	.82777	.82938	.83098	.83258	.83418	.83578	.83737	.83896
.3	.84055	.84214	.84372	.84530	.84688	.84845	.85003	.85160	.85317	.85473
.4	.85630	.85786	.85942	.86097	.86253	.86408	.86563	.86718	.86872	.87026

N	0	1	2	3	4	5	6	7	8	9
6.5	1.87180	1.87334	1.87487	1.87641	1.87794	1.87947	1.88099	1.88251	1.88403	1.88555
.6	.88707	.88858	.89010	.89160	.89311	.89462	.89612	.89762	.89912	.90061
.7	.90211	.90360	.90509	.90658	.90806	.90954	.91102	.91250	.91398	.91545
.8	.91692	.91839	.91986	.92132	.92279	.92425	.92571	.92716	.92862	.93007
.9	.93152	.93297	.93442	.93586	.93730	.93874	.94018	.94162	.94305	.94448
7.0	1.94591	1.94734	1.94876	1.95019	1.95161	1.95303	1.95445	1.95586	1.95727	1.95869
.1	.96009	.96150	.96291	.96431	.96571	.96711	.96851	.96991	.97130	.97269
.2	.97408	.97547	.97685	.97824	.97962	.98100	.98238	.98376	.98513	.98650
.3	.98787	.98924	.99061	.99198	.99334	.99470	.99606	.99742	.99877	2.00013
.4	2.00148	2.00283	2.00418	2.00553	2.00687	2.00821	2.00956	2.01089	2.01223	.01357
.5	2.01490	2.01624	2.01757	2.01890	2.02022	2.02155	2.02287	2.02419	2.02551	2.02683
.6	.02815	.02946	.03078	.03209	.03340	.03471	.03601	.03732	.03862	.03992
.7	.04122	.04252	.04381	.04511	.04640	.04769	.04898	.05027	.05156	.05284
.8	.05412	.05540	.05668	.05796	.05924	.06051	.06179	.06306	.06433	.06560
.9	.06686	.06813	.06939	.07065	.07191	.07317	.07443	.07568	.07694	.07819
8.0	2.07944	2.08069	2.08194	2.08318	2.08443	2.08567	2.08691	2.08815	2.08939	2.09063
.1	.09186	.09310	.09433	.09556	.09679	.09802	.09924	.10047	.10169	.10291
.2	.10413	.10535	.10657	.10779	.10900	.11021	.11142	.11263	.11384	.11505
.3	.11626	.11746	.11866	.11986	.12106	.12226	.12346	.12465	.12585	.12704
.4	.12823	.12942	.13061	.13180	.13298	.13417	.13535	.13653	.13771	.13889
.5	2.14007	2.14124	2.14242	2.14359	2.14476	2.14593	2.14710	2.14827	2.14943	2.15060
.6	.15176	.15292	.15409	.15524	.15640	.15756	.15871	.15987	.16102	.16217
.7	.16332	.16447	.16562	.16677	.16791	.16905	.17020	.17134	.17248	.17361
.8	.17475	.17589	.17702	.17816	.17929	.18042	.18155	.18267	.18380	.18493
.9	.18605	.18717	.18830	.18942	.19054	.19165	.19277	.19389	.19500	.19611
9.0	2.19722	2.19834	2.19944	2.20055	2.20166	2.20276	2.20387	2.20497	2.20607	2.20717
.1	.20827	.20937	.21047	.21157	.21266	.21375	.21485	.21594	.21703	.21812
.2	.21920	.22029	.22138	.22246	.22354	.22462	.22570	.22678	.22786	.22894
.3	.23001	.23109	.23216	.23324	.23431	.23538	.23645	.23751	.23858	.23965
.4	.24071	.24177	.24284	.24390	.24496	.24601	.24707	.24813	.24918	.25024
.5	2.25129	2.25234	2.25339	2.25444	2.25549	2.25654	2.25759	2.25863	2.25968	2.26072
.6	.26176	.26280	.26384	.26488	.26592	.26696	.26799	.26903	.27006	.27109
.7	.27213	.27316	.27419	.27521	.27624	.27727	.27829	.27932	.28034	.28136
.8	.28238	.28340	.28442	.28544	.28646	.28747	.28849	.28950	.29051	.29152
.9	.29253	.29354	.29455	.29556	.29657	.29757	.29858	.29958	.30058	.30158

10.0—49.9

10.	2.30259	2.31254	2.32239	2.33214	2.34181	2.35138	2.36085	2.37024	2.37955	2.38876
11.	.39790	.40695	.41591	.42480	.43361	.44235	.45101	.45959	.46810	.47654
12.	.48491	.49321	.50144	.50960	.51770	.52573	.53370	.54160	.54945	.55723
13.	.56495	.57261	.58022	.58776	.59525	.60269	.61007	.61740	.62467	.63189
14.	.63906	.64617	.65324	.66026	.66723	.67415	.68102	.68785	.69463	.70136
15.	2.70805	2.71469	2.72130	2.72785	2.73437	2.74084	2.74727	2.75366	2.76001	2.76632
16.	.77259	.77882	.78501	.79117	.79728	.80336	.80940	.81541	.82138	.82731
17.	.83321	.83908	.84491	.85071	.85647	.86220	.86790	.87356	.87920	.88480
18.	.89037	.89591	.90142	.90690	.91235	.91777	.92316	.92852	.93386	.93916
19.	.94444	.94969	.95491	.96011	.96527	.97041	.97553	.98062	.98568	.99072
20.	2.99573	3.00072	3.00568	3.01062	3.01553	3.02042	3.02529	3.03013	3.03495	3.03975
21.	3.04452	.04927	.05400	.05871	.06339	.06805	.07269	.07731	.08191	.08649
22.	.09104	.09558	.10009	.10459	.10906	.11352	.11795	.12236	.12676	.13114
23.	.13549	.13983	.14415	.14845	.15274	.15700	.16125	.16548	.16969	.17388
24.	.17805	.18221	.18635	.19048	.19458	.19867	.20275	.20680	.21084	.21487
25.	3.21888	3.22287	3.22684	3.23080	3.23475	3.23868	3.24259	3.24649	3.25037	3.25424
26.	.25810	.26194	.26576	.26957	.27336	.27714	.28091	.28466	.28840	.29213
27.	.29584	.29953	.30322	.30689	.31054	.31419	.31782	.32143	.32504	.32863
28.	.33220	.33577	.33932	.34286	.34639	.34990	.35341	.35690	.36038	.36384
29.	.36730	.37074	.37417	.37759	.38099	.38439	.38777	.39115	.39451	.39786
30.	3.40120	3.40453	3.40784	3.41115	3.41444	3.41773	3.42100	3.42426	3.42751	3.43076
31.	.43399	.43721	.44042	.44362	.44681	.44999	.45316	.45632	.45947	.46261
32.	.46574	.46886	.47197	.47507	.47816	.48124	.48431	.48738	.49043	.49347
33.	.49651	.49953	.50255	.50556	.50856	.51155	.51453	.51750	.52046	.52342
34.	.52636	.52930	.53223	.53515	.53806	.54096	.54385	.54674	.54962	.55249
35.	3.55535	3.55820	3.56105	3.56388	3.56671	3.56953	3.57235	3.57515	3.57795	3.58074
36.	.58352	.58629	.58906	.59182	.59457	.59731	.60005	.60278	.60550	.60821
37.	.61092	.61362	.61631	.61899	.62167	.62434	.62700	.62966	.63231	.63495
38.	.63759	.64021	.64284	.64545	.64806	.65066	.65325	.65584	.65842	.66099
39.	.66356	.66612	.66868	.67122	.67377	.67630	.67883	.68135	.68387	.68638
40.	3.68888	3.69138	3.69387	3.69635	3.69883	3.70130	3.70377	3.70623	3.70868	3.71113
41.	.71357	.71601	.71844	.72086	.72328	.72569	.72810	.73050	.73290	.73529
42.	.73767	.74005	.74242	.74479	.74715	.74950	.75185	.75420	.75654	.75887
43.	.76120	.76352	.76584	.76815	.77046	.77276	.77506	.77735	.77963	.78191
44.	.78419	.78646	.78872	.79098	.79324	.79549	.79773	.79997	.80221	.80444
45.	3.80666	3.80888	3.81110	3.81331	3.81551	3.81771	3.81991	3.82210	3.82428	3.82647
46.	.82864	.83081	.83298	.83514	.83730	.83945	.84160	.84374	.84588	.84802
47.	.85015	.85227	.85439	.85651	.85862	.86073	.86283	.86493	.86703	.86912
48.	.87120	.87328	.87536	.87743	.87950	.88156	.88362	.88568	.88773	.88978
49.	.89182	.89386	.89589	.89792	.89995	.90197	.90399	.90600	.90801	.91002

¹ To find the natural logarithm (\log_e) of a number which is a power of ten less or greater than a number given in the Tables: if the number concerned is less, e.g. $\frac{1}{10}$ (10^{-1}), $\frac{1}{100}$ (10^{-2}), $\frac{1}{1000}$ (10^{-3}), etc. subtract from the given logarithm $\log_e 10$, $2 \log_e 10$, $3 \log_e 10$, etc.; if the number concerned is greater e.g. 10 times (10^1), 100 times (10^2), 1000 times (10^3), etc. add to the given logarithm $\log_e 10$, $2 \log_e 10$, $3 \log_e 10$, etc.
Example: $\log_e 0.02 = \log_e 0.2 - \log_e 10$ or $\log_e 2000 = \log_e 200 + \log_e 10$.

N	0	1	2	3	4	5	6	7	8	9
50.	3.91202	3.91402	3.91602	3.91801	3.91999	3.92197	3.92395	3.92593	3.92790	3.92986
51.	.93183	.93378	.93574	.93769	.93964	.94158	.94352	.94546	.94739	.94932
52.	.95124	.95316	.95508	.95700	.95891	.96081	.96272	.96462	.96651	.96840
53.	.97029	.97218	.97406	.97594	.97781	.97968	.98155	.98341	.98527	.98713
54.	.98898	.99083	.99268	.99452	.99636	.99820	4.00003	4.00186	4.00369	4.00551
55.	4.00733	4.00915	4.01096	4.01277	4.01458	4.01638	4.01818	4.01998	4.02177	4.02356
56.	.02535	.02714	.02892	.03069	.03247	.03424	.03601	.03777	.03954	.04130
57.	.04305	.04480	.04655	.04830	.05004	.05178	.05352	.05526	.05699	.05872
58.	.06044	.06217	.06389	.06560	.06732	.06903	.07073	.07244	.07414	.07584
59.	.07754	.07923	.08092	.08261	.08429	.08598	.08766	.08933	.09101	.09268
60.	4.09434	4.09601	4.09767	4.09933	4.10099	4.10264	4.10429	4.10594	4.10759	4.10923
61.	.11087	.11251	.11415	.11578	.11741	.11904	.12066	.12228	.12390	.12552
62.	.12713	.12875	.13036	.13196	.13357	.13517	.13677	.13836	.13996	.14155
63.	.14313	.14472	.14630	.14789	.14946	.15104	.15261	.15418	.15575	.15732
64.	.15888	.16044	.16200	.16356	.16511	.16667	.16821	.16976	.17131	.17285
65.	4.17439	4.17592	4.17746	4.17899	4.18052	4.18205	4.18358	4.18510	4.18662	4.18814
66.	.18965	.19117	.19268	.19419	.19570	.19720	.19870	.20020	.20170	.20320
67.	.20469	.20618	.20767	.20916	.21065	.21213	.21361	.21509	.21656	.21804
68.	.21951	.22098	.22244	.22391	.22537	.22683	.22829	.22975	.23120	.23266
69.	.23411	.23555	.23700	.23844	.23989	.24133	.24276	.24420	.24563	.24707
70.	4.24850	4.24992	4.25135	4.25277	4.25419	4.25561	4.25703	4.25845	4.25986	4.26127
71.	.26268	.26409	.26549	.26690	.26830	.26970	.27110	.27249	.27388	.27528
72.	.27667	.27805	.27944	.28082	.28221	.28359	.28496	.28634	.28772	.28909
73.	.29046	.29183	.29320	.29456	.29592	.29729	.29865	.30000	.30136	.30271
74.	.30407	.30542	.30676	.30811	.30946	.31080	.31214	.31348	.31482	.31615
75.	4.31749	4.31882	4.32015	4.32149	4.32281	4.32413	4.32546	4.32678	4.32810	4.32942
76.	.33073	.33205	.33336	.33467	.33598	.33729	.33860	.33990	.34120	.34251
77.	.34381	.34510	.34640	.34769	.34899	.35028	.35157	.35286	.35414	.35543
78.	.35671	.35800	.35927	.36055	.36182	.36310	.36437	.36564	.36691	.36818
79.	.36945	.37071	.37198	.37324	.37450	.37576	.37701	.37827	.37952	.38078
80.	4.38203	4.38328	4.38452	4.38577	4.38701	4.38826	4.38950	4.39074	4.39198	4.39321
81.	.39445	.39568	.39692	.39815	.39938	.40060	.40183	.40305	.40428	.40550
82.	.40672	.40794	.40916	.41037	.41159	.41280	.41401	.41522	.41643	.41764
83.	.41884	.42004	.42125	.42245	.42365	.42485	.42604	.42724	.42843	.42963
84.	.43082	.43201	.43319	.43438	.43557	.43675	.43793	.43912	.44030	.44147
85.	4.44265	4.44383	4.44500	4.44617	4.44735	4.44852	4.44969	4.45085	4.45202	4.45318
86.	.45435	.45551	.45667	.45783	.45899	.46014	.46130	.46245	.46361	.46476
87.	.46591	.46706	.46820	.46935	.47050	.47164	.47278	.47392	.47506	.47620
88.	.47734	.47847	.47961	.48074	.48187	.48300	.48413	.48526	.48639	.48751
89.	.48864	.48976	.49088	.49200	.49312	.49424	.49536	.49647	.49758	.49870
90.	4.49981	4.50092	4.50203	4.50314	4.50424	4.50535	4.50645	4.50756	4.50866	4.50976
91.	.51086	.51196	.51305	.51415	.51525	.51634	.51743	.51852	.51961	.52070
92.	.52179	.52287	.52396	.52504	.52613	.52721	.52829	.52937	.53045	.53152
93.	.53260	.53367	.53475	.53582	.53689	.53796	.53903	.54010	.54116	.54223
94.	.54329	.54436	.54542	.54648	.54754	.54860	.54966	.55071	.55177	.55282
95.	4.55388	4.55493	4.55598	4.55703	4.55808	4.55913	4.56017	4.56122	4.56226	4.56331
96.	.56435	.56539	.56643	.56747	.56851	.56954	.57058	.57161	.57265	.57368
97.	.57471	.57574	.57677	.57780	.57883	.57985	.58088	.58190	.58292	.58395
98.	.58497	.58599	.58701	.58802	.58904	.59006	.59107	.59208	.59310	.59411
99.	.59512	.59613	.59714	.59815	.59915	.60016	.60116	.60217	.60317	.60417

0—249

0	∞	0.00000	0.69315	1.09861	1.38629	1.60944	1.79176	1.94591	2.07944	2.19722
1	2.30259	2.39790	2.48491	2.56495	2.63906	2.70805	2.77259	2.83321	2.89037	2.94444
2	2.99573	3.04452	3.09104	3.13549	3.17805	3.21888	3.25810	3.29584	3.33220	3.36730
3	3.40120	.43399	.46574	.49651	.52636	.55535	.58352	.61092	.63759	.66356
4	.68888	.71357	.73767	.76120	.78419	.80666	.82864	.85015	.87120	.89182
5	3.91202	3.93183	3.95124	3.97029	3.98898	4.00733	4.02535	4.04305	4.06044	4.07754
6	4.09434	4.11087	4.12713	4.14313	4.15888	.17439	.18965	.20469	.21951	.23411
7	.24850	.26268	.27667	.29046	.30407	.31749	.33073	.34381	.35671	.36945
8	.38203	.39445	.40672	.41884	.43082	.44265	.45435	.46591	.47734	.48864
9	.49981	.51086	.52179	.53260	.54329	.55388	.56435	.57471	.58497	.59512
10	4.60517	4.61512	4.62497	4.63473	4.64439	4.65396	4.66344	4.67283	4.68213	4.69135
11	.70048	.70953	.71850	.72739	.73620	.74493	.75359	.76217	.77068	.77912
12	.78749	.79579	.80402	.81218	.82028	.82831	.83628	.84419	.85203	.85981
13	.86753	.87520	.88280	.89035	.89784	.90527	.91265	.91998	.92725	.93447
14	.94164	.94876	.95583	.96284	.96981	.97673	.98361	.99043	.99721	5.00395
15	5.01064	5.01728	5.02388	5.03044	5.03695	5.04343	5.04986	5.05625	5.06260	5.06890
16	.07517	.08140	.08760	.09375	.09987	.10595	.11199	.11799	.12396	.12990
17	.13580	.14166	.14749	.15329	.15906	.16479	.17048	.17615	.18178	.18739
18	.19296	.19850	.20401	.20949	.21494	.22036	.22575	.23111	.23644	.24175
19	.24702	.25227	.25750	.26269	.26786	.27300	.27811	.28320	.28827	.29330
20	5.29832	5.30330	5.30827	5.31321	5.31812	5.32301	5.32788	5.33272	5.33754	5.34233
21	.34711	.35186	.35659	.36129	.36598	.37064	.37528	.37990	.38450	.38907
22	.39363	.39816	.40268	.40717	.41165	.41610	.42053	.42495	.42935	.43372
23	.43808	.44242	.44674	.45104	.45532	.45959	.46383	.46806	.47227	.47646
24	.48064	.48480	.48894	.49306	.49717	.50126	.50533	.50939	.51343	.51745

N	0	1	2	3	4	5	6	7	8	9
25	5.52146	5.52545	5.52943	5.53339	5.53733	5.54126	5.54518	5.54908	5.55296	5.55683
26	.56068	.56452	.56834	.57215	.57595	.57973	.58350	.58725	.59099	.59471
27	.59842	.60212	.60580	.60947	.61313	.61677	.62040	.62402	.62762	.63121
28	.63479	.63835	.64191	.64545	.64897	.65249	.65599	.65948	.66296	.66643
29	.66988	.67332	.67675	.68017	.68358	.68698	.69036	.69373	.69709	.70044
30	5.70378	5.70711	5.71043	5.71373	5.71703	5.72031	5.72359	5.72685	5.73010	5.73334
31	.73657	.73979	.74300	.74620	.74939	.75257	.75574	.75890	.76205	.76519
32	.76832	.77144	.77455	.77765	.78074	.78383	.78690	.78996	.79301	.79606
33	.79909	.80212	.80513	.80814	.81114	.81413	.81711	.82008	.82305	.82600
34	.82895	.83188	.83481	.83773	.84064	.84354	.84644	.84932	.85220	.85507
35	5.85793	5.86079	5.86363	5.86647	5.86930	5.87212	5.87493	5.87774	5.88053	5.88332
36	.88610	.88888	.89164	.89440	.89715	.89990	.90263	.90536	.90808	.91080
37	.91350	.91620	.91889	.92158	.92426	.92693	.92959	.93225	.93489	.93754
38	.94017	.94280	.94542	.94803	.95064	.95324	.95584	.95842	.96101	.96358
39	.96615	.96871	.97126	.97381	.97635	.97889	.98141	.98394	.98645	.98896
40	5.99146	5.99396	5.99645	5.99894	6.00141	6.00389	6.00635	6.00881	6.01127	6.01372
41	.01616	.01859	.02102	.02345	.02587	.02828	.03069	.03309	.03548	.03787
42	.04025	.04263	.04501	.04737	.04973	.05209	.05444	.05678	.05912	.06146
43	.06379	.06611	.06843	.07074	.07304	.07535	.07764	.07993	.08222	.08450
44	.08677	.08904	.09131	.09357	.09582	.09807	.10032	.10256	.10479	.10702
45	6.10925	6.11147	6.11368	6.11589	6.11810	6.12030	6.12249	6.12468	6.12687	6.12905
46	.13123	.13340	.13556	.13773	.13988	.14204	.14419	.14633	.14847	.15060
47	.15273	.15486	.15698	.15910	.16121	.16331	.16542	.16752	.16961	.17170
48	.17379	.17587	.17794	.18002	.18208	.18415	.18621	.18826	.19032	.19236
49	.19441	.19644	.19848	.20051	.20254	.20456	.20658	.20859	.21060	.21261
50	6.21461	6.21661	6.21860	6.22059	6.22258	6.22456	6.22654	6.22851	6.23048	6.23245
51	.23441	.23637	.23832	.24028	.24222	.24417	.24611	.24804	.24998	.25190
52	.25383	.25575	.25767	.25958	.26149	.26340	.26530	.26720	.26910	.27099
53	.27288	.27476	.27664	.27852	.28040	.28227	.28413	.28600	.28786	.28972
54	.29157	.29342	.29527	.29711	.29895	.30079	.30262	.30445	.30628	.30810
55	6.30992	6.31173	6.31355	6.31536	6.31716	6.31897	6.32077	6.32257	6.32436	6.32615
56	.32794	.32972	.33150	.33328	.33505	.33683	.33859	.34036	.34212	.34388
57	.34564	.34739	.34914	.35089	.35263	.35437	.35611	.35784	.35957	.36130
58	.36303	.36475	.36647	.36819	.36990	.37161	.37332	.37502	.37673	.37843
59	.38012	.38182	.38351	.38519	.38688	.38856	.39024	.39192	.39359	.39526
60	6.39693	6.39859	6.40026	6.40192	6.40357	6.40523	6.40688	6.40853	6.41017	6.41182
61	.41346	.41510	.41673	.41836	.41999	.42162	.42325	.42487	.42649	.42811
62	.42972	.43133	.43294	.43455	.43615	.43775	.43935	.44095	.44254	.44413
63	.44572	.44731	.44889	.45047	.45205	.45362	.45520	.45677	.45834	.45990
64	.46147	.46303	.46459	.46614	.46770	.46925	.47080	.47235	.47389	.47543
65	6.47697	6.47851	6.48004	6.48158	6.48311	6.48464	6.48616	6.48768	6.48920	6.49072
66	.49224	.49375	.49527	.49677	.49828	.49979	.50129	.50279	.50429	.50578
67	.50728	.50877	.51026	.51175	.51323	.51471	.51619	.51767	.51915	.52062
68	.52209	.52356	.52503	.52649	.52796	.52942	.53088	.53233	.53379	.53524
69	.53669	.53814	.53959	.54103	.54247	.54391	.54535	.54679	.54822	.54965
70	6.55108	6.55251	6.55393	6.55536	6.55678	6.55820	6.55962	6.56103	6.56244	6.56386
71	.56526	.56667	.56808	.56948	.57088	.57228	.57368	.57508	.57647	.57786
72	.57925	.58064	.58203	.58341	.58479	.58617	.58755	.58893	.59030	.59167
73	.59304	.59441	.59578	.59715	.59851	.59987	.60123	.60259	.60394	.60530
74	.60665	.60800	.60935	.61070	.61204	.61338	.61473	.61607	.61740	.61874
75	6.62007	6.62141	6.62274	6.62407	6.62539	6.62672	6.62804	6.62936	6.63068	6.63200
76	.63332	.63463	.63595	.63726	.63857	.63988	.64118	.64249	.64379	.64509
77	.64639	.64769	.64898	.65028	.65157	.65286	.65415	.65544	.65673	.65801
78	.65929	.66058	.66185	.66313	.66441	.66568	.66696	.66823	.66950	.67077
79	.67203	.67330	.67456	.67582	.67708	.67834	.67960	.68085	.68211	.68336
80	6.68461	6.68586	6.68711	6.68835	6.68960	6.69084	6.69208	6.69332	6.69456	6.69580
81	.69703	.69827	.69950	.70073	.70196	.70319	.70441	.70564	.70686	.70808
82	.70930	.71052	.71174	.71296	.71417	.71538	.71659	.71780	.71901	.72022
83	.72143	.72263	.72383	.72503	.72623	.72743	.72863	.72982	.73102	.73221
84	.73340	.73459	.73578	.73697	.73815	.73934	.74052	.74170	.74288	.74406
85	6.74524	6.74641	6.74759	6.74876	6.74993	6.75110	6.75227	6.75344	6.75460	6.75577
86	.75693	.75809	.75926	.76041	.76157	.76273	.76388	.76504	.76619	.76734
87	.76849	.76964	.77079	.77194	.77308	.77422	.77537	.77651	.77765	.77878
88	.77992	.78106	.78219	.78333	.78446	.78559	.78672	.78784	.78897	.79010
89	.79122	.79234	.79347	.79459	.79571	.79682	.79794	.79906	.80017	.80128
90	6.80239	6.80351	6.80461	6.80572	6.80683	6.80793	6.80904	6.81014	6.81124	6.81235
91	.81344	.81454	.81564	.81674	.81783	.81892	.82002	.82111	.82220	.82329
92	.82437	.82546	.82655	.82763	.82871	.82979	.83087	.83195	.83303	.83411
93	.83518	.83626	.83733	.83841	.83948	.84055	.84162	.84268	.84375	.84482
94	.84588	.84694	.84801	.84907	.85013	.85118	.85224	.85330	.85435	.85541
95	6.85646	6.85751	6.85857	6.85961	6.86066	6.86171	6.86276	6.86380	6.86485	6.86589
96	.86693	.86797	.86901	.87005	.87109	.87213	.87316	.87420	.87523	.87626
97	.87730	.87833	.87936	.88038	.88141	.88244	.88346	.88449	.88551	.88653
98	.88755	.88857	.88959	.89061	.89163	.89264	.89366	.89467	.89568	.89669
99	.89770	.89871	.89972	.90073	.90174	.90274	.90375	.90475	.90575	.90675

¹) To find the natural logarithm (\log_e) of a number which is a power of ten less or greater than a number given in the Tables: if the number concerned is less, e.g. $\frac{1}{10}$ (10^{-1}), $\frac{1}{100}$ (10^{-2}), $\frac{1}{1000}$ (10^{-3}), etc. *subtract* from the given logarithm $\log_e 10$, $2 \log_e 10$, $3 \log_e 10$, etc.; if the number concerned is greater, e.g. 10 times (10^1), 100 times (10^2), 1000 times (10^3), etc. *add* to the given logarithm $\log_e 10$, $2 \log_e 10$, $3 \log_e 10$, etc.
Example: $\log_e 0.02 = \log_e 0.2 - \log_e 10$ or $\log_e 2000 = \log_e 200 + \log_e 10$.

x	e^x	$\log_{10}(e^x)$	e^{-x}	x	e^x	$\log_{10}(e^x)$	e^{-x}	x	e^x	$\log_{10}(e^x)$	e^{-x}
0.00	1.0000	0.00000	1.000000	0.50	1.6487	0.21715	0.606531	1.00	2.7183	0.43429	0.367879
0.01	1.0101	.00434	0.990050	0.51	1.6653	.22149	.600496	1.01	2.7456	.43864	.364219
0.02	1.0202	.00869	.980199	0.52	1.6820	.22583	.594521	1.02	2.7732	.44298	.360595
0.03	1.0305	.01303	.970446	0.53	1.6989	.23018	.588605	1.03	2.8011	.44732	.357007
0.04	1.0408	.01737	.960789	0.54	1.7160	.23452	.582748	1.04	2.8292	.45167	.353455
0.05	1.0513	0.02171	0.951229	0.55	1.7333	0.23886	0.576950	1.05	2.8577	0.45601	0.349938
0.06	1.0618	.02606	.941765	0.56	1.7507	.24320	.571209	1.06	2.8864	.46035	.346456
0.07	1.0725	.03040	.932394	0.57	1.7683	.24755	.565525	1.07	2.9154	.46470	.343009
0.08	1.0833	.03474	.923116	0.58	1.7860	.25189	.559898	1.08	2.9447	.46904	.339596
0.09	1.0942	.03909	.913931	0.59	1.8040	.25623	.554327	1.09	2.9743	.47338	.336216
0.10	1.1052	0.04343	0.904837	0.60	1.8221	0.26058	0.548812	1.10	3.0042	0.47772	0.332871
0.11	1.1163	.04777	.895834	0.61	1.8404	.26492	.543351	1.11	3.0344	.48207	.329559
0.12	1.1275	.05212	.886920	0.62	1.8589	.26926	.537944	1.12	3.0649	.48641	.326280
0.13	1.1388	.05646	.878095	0.63	1.8776	.27361	.532592	1.13	3.0957	.49075	.323033
0.14	1.1503	.06080	.869358	0.64	1.8965	.27795	.527292	1.14	3.1268	.49510	.319819
0.15	1.1618	0.06514	0.860708	0.65	1.9155	0.28229	0.522046	1.15	3.1582	0.49944	0.316637
0.16	1.1735	.06949	.852144	0.66	1.9348	.28663	.516851	1.16	3.1899	.50378	.313486
0.17	1.1853	.07383	.843665	0.67	1.9542	.29098	.511709	1.17	3.2220	.50812	.310367
0.18	1.1972	.07817	.835270	0.68	1.9739	.29532	.506617	1.18	3.2544	.51247	.307279
0.19	1.2092	.08252	.826959	0.69	1.9937	.29966	.501576	1.19	3.2871	.51681	.304221
0.20	1.2214	0.08686	0.818731	0.70	2.0138	0.30401	0.496585	1.20	3.3201	0.52115	0.301194
0.21	1.2337	.09120	.810584	0.71	2.0340	.30835	.491644	1.21	3.3535	.52550	.298197
0.22	1.2461	.09554	.802519	0.72	2.0544	.31269	.486752	1.22	3.3872	.52984	.295230
0.23	1.2586	.09989	.794534	0.73	2.0751	.31703	.481909	1.23	3.4212	.53418	.292293
0.24	1.2712	.10423	.786628	0.74	2.0959	.32138	.477114	1.24	3.4556	.53853	.289384
0.25	1.2840	0.10857	0.778801	0.75	2.1170	0.32572	0.472367	1.25	3.4903	0.54287	0.286505
0.26	1.2969	.11292	.771052	0.76	2.1383	.33006	.467666	1.26	3.5254	.54721	.283654
0.27	1.3100	.11726	.763379	0.77	2.1598	.33441	.463013	1.27	3.5609	.55155	.280832
0.28	1.3231	.12160	.755784	0.78	2.1815	.33875	.458406	1.28	3.5966	.55590	.278037
0.29	1.3364	.12595	.748264	0.79	2.2034	.34309	.453845	1.29	3.6328	.56024	.275271
0.30	1.3499	0.13029	0.740818	0.80	2.2255	0.34744	0.449329	1.30	3.6693	0.56458	0.272532
0.31	1.3634	.13463	.733447	0.81	2.2479	.35178	.444858	1.31	3.7062	.56893	.269820
0.32	1.3771	.13897	.726149	0.82	2.2705	.35612	.440432	1.32	3.7434	.57327	.267135
0.33	1.3910	.14332	.718924	0.83	2.2933	.36046	.436049	1.33	3.7810	.57761	.264477
0.34	1.4049	.14766	.711770	0.84	2.3164	.36481	.431711	1.34	3.8190	.58195	.261846
0.35	1.4191	0.15200	0.704688	0.85	2.3396	0.36915	0.427415	1.35	3.8574	0.58630	0.259240
0.36	1.4333	.15635	.697676	0.86	2.3632	.37349	.423162	1.36	3.8962	.59064	.256661
0.37	1.4477	.16069	.690734	0.87	2.3869	.37784	.418952	1.37	3.9354	.59498	.254107
0.38	1.4623	.16503	.683861	0.88	2.4109	.38218	.414783	1.38	3.9749	.59933	.251579
0.39	1.4770	.16937	.677057	0.89	2.4351	.38652	.410656	1.39	4.0149	.60367	.249075
0.40	1.4918	0.17372	0.670320	0.90	2.4596	0.39087	0.406570	1.40	4.0552	0.60801	0.246597
0.41	1.5068	.17806	.663650	0.91	2.4843	.39521	.402524	1.41	4.0960	.61236	.244143
0.42	1.5220	.18240	.657047	0.92	2.5093	.39955	.398519	1.42	4.1371	.61670	.241714
0.43	1.5373	.18675	.650509	0.93	2.5345	.40389	.394554	1.43	4.1787	.62104	.239309
0.44	1.5527	.19109	.644036	0.94	2.5600	.40824	.390628	1.44	4.2207	.62538	.236928
0.45	1.5683	0.19543	0.637628	0.95	2.5857	0.41258	0.386741	1.45	4.2631	0.62973	0.234570
0.46	1.5841	.19978	.631284	0.96	2.6117	.41692	.382893	1.46	4.3060	.63407	.232236
0.47	1.6000	.20412	.625002	0.97	2.6379	.42127	.379083	1.47	4.3492	.63841	.229925
0.48	1.6161	.20846	.618783	0.98	2.6645	.42561	.375311	1.48	4.3929	.64276	.227638
0.49	1.6323	.21280	.612626	0.99	2.6912	.42995	.371577	1.49	4.4371	.64710	.225373

x	e^x	$\log_{10}(e^x)$	e^{-x}	x	e^x	$\log_{10}(e^x)$	e^{-x}	x	e^x	$\log_{10}(e^x)$	e^{-x}
1.50	4.4817	0.65144	0.223130	2.00	7.3891	0.86859	0.135335	2.50	12.182	1.08574	0.082085
1.51	4.5267	.65578	.220910	2.01	7.4633	.87293	.133989	2.51	12.305	1.09008	.081268
1.52	4.5722	.66013	.218712	2.02	7.5383	.87727	.132655	2.52	12.429	1.09442	.080460
1.53	4.6182	.66447	.216536	2.03	7.6141	.88162	.131336	2.53	12.554	1.09877	.079659
1.54	4.6646	.66881	.214381	2.04	7.6906	.88596	.130029	2.54	12.680	1.10311	.078866
1.55	4.7115	0.67316	0.212248	2.05	7.7679	0.89030	0.128735	2.55	12.807	1.10745	0.078082
1.56	4.7588	.67750	.210136	2.06	7.8460	.89465	.127454	2.56	12.936	1.11179	.077305
1.57	4.8066	.68184	.208045	2.07	7.9248	.89899	.126186	2.57	13.066	1.11614	.076536
1.58	4.8550	.68619	.205975	2.08	8.0045	.90333	.124930	2.58	13.197	1.12048	.075774
1.59	4.9037	.69053	.203926	2.09	8.0849	.90768	.123687	2.59	13.330	1.12482	.075020
1.60	4.9530	0.69487	0.201897	2.10	8.1662	0.91202	0.122456	2.60	13.464	1.12917	0.074274
1.61	5.0028	.69921	.199888	2.11	8.2482	.91636	.121238	2.61	13.599	1.13351	.073535
1.62	5.0531	.70356	.197899	2.12	8.3311	.92070	.120032	2.62	13.736	1.13785	.072803
1.63	5.1039	.70790	.195930	2.13	8.4149	.92505	.118837	2.63	13.874	1.14219	.072078
1.64	5.1552	.71224	.193980	2.14	8.4994	.92939	.117655	2.64	14.013	1.14654	.071361
1.65	5.2070	0.71659	0.192050	2.15	8.5849	0.93373	0.116484	2.65	14.154	1.15088	0.070651
1.66	5.2593	.72093	.190139	2.16	8.6711	.93808	.115325	2.66	14.296	1.15522	.069948
1.67	5.3122	.72527	.188247	2.17	8.7583	.94242	.114178	2.67	14.440	1.15957	.069252
1.68	5.3656	.72961	.186374	2.18	8.8463	.94676	.113042	2.68	14.585	1.16391	.068563
1.69	5.4195	.73396	.184520	2.19	8.9352	.95110	.111917	2.69	14.732	1.16825	.067881
1.70	5.4739	0.73830	0.182684	2.20	9.0250	0.95545	0.110803	2.70	14.880	1.17260	0.067206
1.71	5.5290	.74264	.180866	2.21	9.1157	.95979	.109701	2.71	15.029	1.17694	.066537
1.72	5.5845	.74699	.179066	2.22	9.2073	.96413	.108609	2.72	15.180	1.18128	.065875
1.73	5.6407	.75133	.177284	2.23	9.2999	.96848	.107528	2.73	15.333	1.18562	.065219
1.74	5.6973	.75567	.175520	2.24	9.3933	.97282	.106459	2.74	15.487	1.18997	.064570
1.75	5.7546	0.76002	0.173774	2.25	9.4877	0.97716	0.105399	2.75	15.643	1.19431	0.063928
1.76	5.8124	.76436	.172045	2.26	9.5831	.98151	.104350	2.76	15.800	1.19865	.063292
1.77	5.8709	.76870	.170333	2.27	9.6794	.98585	.103312	2.77	15.959	1.20300	.062662
1.78	5.9299	.77304	.168638	2.28	9.7767	.99019	.102284	2.78	16.119	1.20734	.062039
1.79	5.9895	.77739	.166960	2.29	9.8749	.99453	.101266	2.79	16.281	1.21168	.061421
1.80	6.0496	0.78173	0.165299	2.30	9.9742	0.99888	0.100259	2.80	16.445	1.21602	0.060810
1.81	6.1104	.78607	.163654	2.31	10.074	1.00322	.099261	2.81	16.610	1.22037	.060205
1.82	6.1719	.79042	.162026	2.32	10.176	1.00756	.098274	2.82	16.777	1.22471	.059606
1.83	6.2339	.79476	.160414	2.33	10.278	1.01191	.097296	2.83	16.945	1.22905	.059013
1.84	6.2965	.79910	.158817	2.34	10.381	1.01625	.096328	2.84	17.116	1.23340	.058426
1.85	6.3598	0.80344	0.157237	2.35	10.486	1.02059	0.095369	2.85	17.288	1.23774	0.057844
1.86	6.4237	.80779	.155673	2.36	10.591	1.02493	.094420	2.86	17.462	1.24208	.057269
1.87	6.4883	.81213	.154124	2.37	10.697	1.02928	.093481	2.87	17.637	1.24643	.056699
1.88	6.5535	.81647	.152590	2.38	10.805	1.03362	.092551	2.88	17.814	1.25077	.056135
1.89	6.6194	.82082	.151072	2.39	10.913	1.03796	.091630	2.89	17.993	1.25511	.055576
1.90	6.6859	0.82516	0.149569	2.40	11.023	1.04231	0.090718	2.90	18.174	1.25945	0.055023
1.91	6.7531	.82950	.148080	2.41	11.134	1.04665	.089815	2.91	18.357	1.26380	.054476
1.92	6.8210	.83385	.146607	2.42	11.246	1.05099	.088922	2.92	18.541	1.26814	.053934
1.93	6.8895	.83819	.145148	2.43	11.359	1.05534	.088037	2.93	18.728	1.27248	.053397
1.94	6.9588	.84253	.143704	2.44	11.473	1.05968	.087161	2.94	18.916	1.27683	.052866
1.95	7.0287	0.84687	0.142274	2.45	11.588	1.06402	0.086294	2.95	19.106	1.28117	0.052340
1.96	7.0993	.85122	.140858	2.46	11.705	1.06836	.085435	2.96	19.298	1.28551	.051819
1.97	7.1707	.85556	.139457	2.47	11.822	1.07271	.084585	2.97	19.492	1.28985	.051303
1.98	7.2427	.85990	.138069	2.48	11.941	1.07705	.083743	2.98	19.688	1.29420	.050793
1.99	7.3155	.86425	.136695	2.49	12.061	1.08139	.082910	2.99	19.886	1.29854	.050287

x	e^x	$\log_{10}(e^x)$	e^{-x}	x	e^x	$\log_{10}(e^x)$	e^{-x}	x	e^x	$\log_{10}(e^x)$	e^{-x}
3.00	20.086	1.30288	0.049787	3.50	33.115	1.52003	0.030197	4.00	54.598	1.73718	0.018316
3.01	20.287	1.30723	.049292	3.51	33.448	1.52437	.029897	4.01	55.147	1.74152	.018133
3.02	20.491	1.31157	.048801	3.52	33.784	1.52872	.029599	4.02	55.701	1.74586	.017953
3.03	20.697	1.31591	.048316	3.53	34.124	1.53306	.029305	4.03	56.261	1.75021	.017774
3.04	20.905	1.32026	.047835	3.54	34.467	1.53740	.029013	4.04	56.826	1.75455	.017597
3.05	21.115	1.32460	0.047359	3.55	34.813	1.54175	0.028725	4.05	57.397	1.75889	0.017422
3.06	21.328	1.32894	.046888	3.56	35.163	1.54609	.028439	4.06	57.974	1.76324	.017249
3.07	21.542	1.33328	.046421	3.57	35.517	1.55043	.028156	4.07	58.557	1.76758	.017077
3.08	21.758	1.33763	.045959	3.58	35.874	1.55477	.027876	4.08	59.145	1.77192	.016907
3.09	21.977	1.34197	.045502	3.59	36.234	1.55912	.027598	4.09	59.740	1.77626	.016739
3.10	22.198	1.34631	0.045049	3.60	36.598	1.56346	0.027324	4.10	60.340	1.78061	0.016573
3.11	22.421	1.35066	.044601	3.61	36.966	1.56780	.027052	4.11	60.947	1.78495	.016408
3.12	22.646	1.35500	.044157	3.62	37.338	1.57215	.026783	4.12	61.559	1.78929	.016245
3.13	22.874	1.35934	.043718	3.63	37.713	1.57649	.026516	4.13	62.178	1.79364	.016083
3.14	23.104	1.36368	.043283	3.64	38.092	1.58083	.026252	4.14	62.803	1.79798	.015923
3.15	23.336	1.36803	0.042852	3.65	38.475	1.58517	0.025991	4.15	63.434	1.80232	0.015764
3.16	23.571	1.37237	.042426	3.66	38.861	1.58952	.025733	4.16	64.072	1.80667	.015608
3.17	23.807	1.37671	.042004	3.67	39.252	1.59386	.025476	4.17	64.715	1.81101	.015452
3.18	24.047	1.38106	.041586	3.68	39.646	1.59820	.025223	4.18	65.366	1.81535	.015299
3.19	24.288	1.38540	.041172	3.69	40.045	1.60255	.024972	4.19	66.023	1.81969	.015146
3.20	24.533	1.38974	0.040762	3.70	40.447	1.60689	0.024724	4.20	66.686	1.82404	0.014996
3.21	24.779	1.39409	.040357	3.71	40.854	1.61123	.024478	4.21	67.357	1.82838	.014846
3.22	25.028	1.39843	.039955	3.72	41.264	1.61558	.024234	4.22	68.033	1.83272	.014699
3.23	25.280	1.40277	.039557	3.73	41.679	1.61992	.023993	4.23	68.717	1.83707	.014552
3.24	25.534	1.40711	.039164	3.74	42.098	1.62426	.023754	4.24	69.408	1.84141	.014408
3.25	25.790	1.41146	0.038774	3.75	42.521	1.62860	0.023518	4.25	70.105	1.84575	0.014264
3.26	26.050	1.41580	.038388	3.76	42.948	1.63295	.023284	4.26	70.810	1.85009	.014122
3.27	26.311	1.42014	.038006	3.77	43.380	1.63729	.023052	4.27	71.522	1.85444	.013982
3.28	26.576	1.42449	.037628	3.78	43.816	1.64163	.022823	4.28	72.240	1.85878	.013843
3.29	26.843	1.42883	.037254	3.79	44.256	1.64598	.022596	4.29	72.966	1.86312	.013705
3.30	27.113	1.43317	0.036883	3.80	44.701	1.65032	0.022371	4.30	73.700	1.86747	0.013569
3.31	27.385	1.43751	.036516	3.81	45.150	1.65466	.022148	4.31	74.440	1.87181	.013434
3.32	27.660	1.44186	.036153	3.82	45.604	1.65900	.021928	4.32	75.189	1.87615	.013300
3.33	27.938	1.44620	.035793	3.83	46.063	1.66335	.021710	4.33	75.944	1.88050	.013168
3.34	28.219	1.45054	.035437	3.84	46.525	1.66769	.021494	4.34	76.708	1.88484	.013037
3.35	28.503	1.45489	0.035084	3.85	46.993	1.67203	0.021280	4.35	77.478	1.88918	0.012907
3.36	28.789	1.45923	.034735	3.86	47.465	1.67638	.021068	4.36	78.257	1.89352	.012778
3.37	29.079	1.46357	.034390	3.87	47.942	1.68072	.020858	4.37	79.044	1.89787	.012651
3.38	29.371	1.46792	.034047	3.88	48.424	1.68506	.020651	4.38	79.838	1.90221	.012525
3.39	29.666	1.47226	.033709	3.89	48.911	1.68941	.020445	4.39	80.640	1.90655	.012401
3.40	29.964	1.47660	0.033373	3.90	49.402	1.69375	0.020242	4.40	81.451	1.91090	0.012277
3.41	30.265	1.48094	.033041	3.91	49.899	1.69809	.020041	4.41	82.269	1.91524	.012155
3.42	30.569	1.48529	.032712	3.92	50.400	1.70243	.019841	4.42	83.096	1.91958	.012034
3.43	30.877	1.48963	.032387	3.93	50.907	1.70678	.019644	4.43	83.931	1.92392	.011914
3.44	31.187	1.49397	.032065	3.94	51.419	1.71112	.019448	4.44	84.775	1.92827	.011796
3.45	31.500	1.49832	0.031746	3.95	51.935	1.71546	0.019255	4.45	85.627	1.93261	0.011679
3.46	31.817	1.50266	.031430	3.96	52.457	1.71981	.019063	4.46	86.488	1.93695	.011562
3.47	32.137	1.50700	.031117	3.97	52.985	1.72415	.018873	4.47	87.357	1.94130	.011447
3.48	32.460	1.51134	.030807	3.98	53.517	1.72849	.018686	4.48	88.235	1.94564	.011333
3.49	32.786	1.51569	.030501	3.99	54.055	1.73283	.018500	4.49	89.121	1.94998	.011221

x	e^x	$\log_{10}(e^x)$	e^{-x}	x	e^x	$\log_{10}(e^x)$	e^{-x}	x	e^x	$\log_{10}(e^x)$	e^{-x}
4.50	90.017	1.95433	0.011109	5.00	148.41	2.17147	0.006738	5.0	148.41	2.17147	0.006738
4.51	90.922	1.95867	.010998	5.01	149.90	2.17582	.006671	5.1	164.02	2.21490	.006097
4.52	91.836	1.96301	.010889	5.02	151.41	2.18016	.006605	5.2	181.27	2.25833	.005517
4.53	92.759	1.96735	.010781	5.03	152.93	2.18450	.006539	5.3	200.34	2.30176	.004992
4.54	93.691	1.97170	.010673	5.04	154.47	2.18884	.006474	5.4	221.41	2.34519	.004517
4.55	94.632	1.97604	0.010567	5.05	156.02	2.19319	0.006409	5.5	244.69	2.38862	0.004087
4.56	95.583	1.98038	.010462	5.06	157.59	2.19753	.006346	5.6	270.43	2.43205	.003698
4.57	96.544	1.98473	.010358	5.07	159.17	2.20187	.006282	5.7	298.87	2.47548	.003346
4.58	97.514	1.98907	.010255	5.08	160.77	2.20622	.006220	5.8	330.30	2.51891	.003028
4.59	98.494	1.99341	.010153	5.09	162.39	2.21056	.006158	5.9	365.04	2.56234	.002739
4.60	99.484	1.99775	0.010052	5.10	164.02	2.21490	0.006097	6.0	403.43	2.60577	0.002479
4.61	100.48	2.00210	.009952	5.11	165.67	2.21924	.006036	6.1	445.86	2.64920	.002243
4.62	101.49	2.00644	.009853	5.12	167.34	2.22359	.005976	6.2	492.75	2.69263	.002029
4.63	102.51	2.01078	.009755	5.13	169.02	2.22793	.005917	6.3	544.57	2.73606	.001836
4.64	103.54	2.01513	.009658	5.14	170.72	2.23227	.005858	6.4	601.85	2.77948	.001662
4.65	104.58	2.01947	0.009562	5.15	172.43	2.23662	0.005799	6.5	665.14	2.82291	0.001503
4.66	105.64	2.02381	.009466	5.16	174.16	2.24096	.005742	6.6	735.10	2.86634	.001360
4.67	106.70	2.02816	.009372	5.17	175.91	2.24530	.005685	6.7	812.41	2.90977	.001231
4.68	107.77	2.03250	.009279	5.18	177.68	2.24965	.005628	6.8	897.85	2.95320	.001114
4.69	108.85	2.03684	.009187	5.19	179.47	2.25399	.005572	6.9	992.27	2.99663	.001008
4.70	109.95	2.04118	0.009095	5.20	181.27	2.25833	0.005517	7.0	1096.6	3.04006	0.000912
4.71	111.05	2.04553	.009005	5.21	183.09	2.26267	.005462	7.1	1212.0	3.08349	.000825
4.72	112.17	2.04987	.008915	5.22	184.93	2.26702	.005407	7.2	1339.4	3.12692	.000747
4.73	113.30	2.05421	.008826	5.23	186.79	2.27136	.005354	7.3	1480.3	3.17035	.000676
4.74	114.43	2.05856	.008739	5.24	188.67	2.27570	.005300	7.4	1636.0	3.21378	.000611
4.75	115.58	2.06290	0.008652	5.25	190.57	2.28005	0.005248	7.5	1808.0	3.25721	0.000553
4.76	116.75	2.06724	.008566	5.26	192.48	2.28439	.005195	7.6	1998.2	3.30064	.000501
4.77	117.92	2.07158	.008480	5.27	194.42	2.28873	.005144	7.7	2208.3	3.33407	.000453
4.78	119.10	2.07593	.008396	5.28	196.37	2.29307	.005092	7.8	2440.6	3.38750	.000410
4.79	120.30	2.08027	.008312	5.29	198.34	2.29742	.005042	7.9	2697.3	3.43093	.000371
4.80	121.51	2.08461	0.008230	5.30	200.34	2.30176	0.004992	8.0	2981.0	3.47436	0.000336
4.81	122.73	2.08896	.008148	5.31	202.35	2.30610	.004942	8.1	3294.5	3.51779	.000304
4.82	123.97	2.09330	.008067	5.32	204.38	2.31045	.004893	8.2	3641.0	3.56121	.000275
4.83	125.21	2.09764	.007987	5.33	206.44	2.31479	.004844	8.3	4023.9	3.60464	.000249
4.84	126.47	2.10199	.007907	5.34	208.51	2.31913	.004796	8.4	4447.1	3.64807	.000225
4.85	127.74	2.10633	0.007828	5.35	210.61	2.32348	0.004748	8.5	4914.8	3.69150	0.000204
4.86	129.02	2.11067	.007750	5.36	212.72	2.32782	.004701	8.6	5431.7	3.73493	.000184
4.87	130.32	2.11501	.007673	5.37	214.86	2.33216	.004654	8.7	6002.9	3.77836	.000167
4.88	131.63	2.11936	.007597	5.38	217.02	2.33650	.004608	8.8	6634.2	3.82179	.000151
4.89	132.95	2.12370	.007521	5.39	219.20	2.34085	.004562	8.9	7332.0	3.86522	.000136
4.90	134.29	2.12804	0.007447	5.40	221.41	2.34519	0.004517	9.0	8103.1	3.90865	0.000123
4.91	135.64	2.13239	.007372	5.41	223.63	2.34953	.004472	9.1	8955.3	3.95208	.000112
4.92	137.00	2.13673	.007299	5.42	225.88	2.35388	.004427	9.2	9897.1	3.99551	.000101
4.93	138.38	2.14107	.007227	5.43	228.15	2.35822	.004383	9.3	10938	4.03894	.000091
4.94	139.77	2.14541	.007155	5.44	230.44	2.36256	.004339	9.4	12088	4.08237	.000083
4.95	141.17	2.14976	0.007083	5.45	232.76	2.36690	0.004296	9.5	13360	4.12580	0.000075
4.96	142.59	2.15410	.007013	5.46	235.10	2.37125	.004254	9.6	14765	4.16923	.000068
4.97	144.03	2.15844	.006943	5.47	237.46	2.37559	.004211	9.7	16318	4.21266	.000061
4.98	145.47	2.16279	.006874	5.48	239.85	2.37993	.004169	9.8	18034	4.25609	.000056
4.99	146.94	2.16713	.006806	5.49	242.26	2.38428	.004128	9.9	19930	4.29952	.000050
				5.50	244.69	2.38862	.004087	10.0	22026	4.34294	.000045

$\sqrt{100n} = 10\sqrt{n}$

$\sqrt{1000n} = 10\sqrt{10n}$

$\sqrt{\frac{n}{10}} = \frac{1}{10}\sqrt{10n}$

$\sqrt{\frac{n}{100}} = \frac{1}{10}\sqrt{n}$

$\sqrt{\frac{n}{1000}} = \frac{1}{100}\sqrt{10n}$

<i>n</i>	<i>n</i> ²	\sqrt{n}	$\sqrt{10n}$	<i>n</i>	<i>n</i> ²	\sqrt{n}	$\sqrt{10n}$	<i>n</i>	<i>n</i> ²	\sqrt{n}	$\sqrt{10n}$	<i>n</i>	<i>n</i> ²	\sqrt{n}	$\sqrt{10n}$
1	1	1.000 000	3.162 278	70	4 900	8.366 600	26.45751	140	19 600	11.83216	37.41657	210	44 100	14.49138	45.82576
2	4	1.414 214	4.472 136	71	5 041	8.426 150	26.64583	141	19 881	11.87434	37.54997	211	44 521	14.52584	45.93474
3	9	1.732 051	5.477 226	72	5 184	8.485 281	26.83282	142	20 164	11.91638	37.68289	212	44 944	14.56022	46.04346
4	16	2.000 000	6.324 555	73	5 329	8.544 004	27.01851	143	20 449	11.95826	37.81534	213	45 369	14.59452	46.15192
5	25	2.236 068	7.071 068	74	5 476	8.602 325	27.20294	144	20 736	12.00000	37.94733	214	45 796	14.62874	46.26013
6	36	2.449 490	7.745 967	75	5 625	8.660 254	27.38613	145	21 025	12.04159	38.07887	215	46 225	14.66288	46.36809
7	49	2.645 751	8.366 600	76	5 776	8.717 798	27.56810	146	21 316	12.08305	38.20995	216	46 656	14.69694	46.47580
8	64	2.828 427	8.944 272	77	5 929	8.774 964	27.74887	147	21 609	12.12436	38.34058	217	47 089	14.73092	46.58326
9	81	3.000 000	9.486 833	78	6 084	8.831 761	27.92848	148	21 904	12.16553	38.47077	218	47 524	14.76482	46.69047
10	100	3.162 278	10.00000	79	6 241	8.888 194	28.10694	149	22 201	12.20656	38.60052	219	47 961	14.79865	46.79744
11	121	3.316 625	10.48809	80	6 400	8.944 272	28.28427	150	22 500	12.24745	38.72983	220	48 400	14.83240	46.90416
12	144	3.464 102	10.95445	81	6 561	9.000 000	28.46050	151	22 801	12.28821	38.85872	221	48 841	14.86607	47.01064
13	169	3.605 551	11.40175	82	6 724	9.055 385	28.63564	152	23 104	12.32883	38.98718	222	49 284	14.89966	47.11688
14	196	3.741 657	11.83216	83	6 889	9.110 434	28.80972	153	23 409	12.36932	39.11521	223	49 729	14.93318	47.22288
15	225	3.872 983	12.24745	84	7 056	9.165 151	28.98275	154	23 716	12.40967	39.24283	224	50 176	14.96663	47.32864
16	256	4.000 000	12.64911	85	7 225	9.219 544	29.15476	155	24 025	12.44990	39.37004	225	50 625	15.00000	47.43416
17	289	4.123 106	13.03840	86	7 396	9.273 618	29.32576	156	24 336	12.49000	39.49684	226	51 076	15.03330	47.53946
18	324	4.242 641	13.41641	87	7 569	9.327 379	29.49576	157	24 649	12.52996	39.62323	227	51 529	15.06652	47.64452
19	361	4.358 899	13.78405	88	7 744	9.380 832	29.66479	158	24 964	12.56981	39.74921	228	51 984	15.09967	47.74935
20	400	4.472 136	14.14214	89	7 921	9.433 981	29.83287	159	25 281	12.60952	39.87480	229	52 441	15.13275	47.85394
21	441	4.582 576	14.49138	90	8 100	9.486 833	30.00000	160	25 600	12.64911	40.00000	230	52 900	15.16575	47.95832
22	484	4.690 416	14.83240	91	8 281	9.539 392	30.16621	161	25 921	12.68858	40.12481	231	53 361	15.19868	48.06246
23	529	4.795 832	15.16575	92	8 464	9.591 663	30.33150	162	26 244	12.72792	40.24922	232	53 824	15.23155	48.16638
24	576	4.898 979	15.49193	93	8 649	9.643 651	30.49590	163	26 569	12.76715	40.37326	233	54 289	15.26434	48.27007
25	625	5.000 000	15.81139	94	8 836	9.695 360	30.65942	164	26 896	12.80625	40.49691	234	54 756	15.29706	48.37355
26	676	5.099 020	16.12452	95	9 025	9.746 794	30.82207	165	27 225	12.84523	40.62019	235	55 225	15.32971	48.47680
27	729	5.196 152	16.43168	96	9 216	9.797 959	30.98387	166	27 556	12.88410	40.74310	236	55 696	15.36229	48.57983
28	784	5.291 503	16.73320	97	9 409	9.848 858	31.14482	167	27 889	12.92285	40.86563	237	56 169	15.39480	48.68265
29	841	5.385 165	17.02939	98	9 604	9.899 495	31.30495	168	28 224	12.96148	40.98780	238	56 644	15.42725	48.78524
30	900	5.477 226	17.32051	99	9 801	9.949 874	31.46427	169	28 561	13.00000	41.10961	239	57 121	15.45962	48.88763
31	961	5.567 764	17.60682	100	10 000	10.00000	31.62278	170	28 900	13.03840	41.23106	240	57 600	15.49193	48.98979
32	1 024	5.656 854	17.88854	101	10 201	10.04988	31.78050	171	29 241	13.07670	41.35215	241	58 081	15.52417	49.09175
33	1 089	5.744 563	18.16590	102	10 404	10.09950	31.93744	172	29 584	13.11488	41.47288	242	58 564	15.55635	49.19350
34	1 156	5.830 952	18.43909	103	10 609	10.14889	32.09361	173	29 929	13.15295	41.59327	243	59 049	15.58846	49.29503
35	1 225	5.916 080	18.70829	104	10 816	10.19804	32.24903	174	30 276	13.19091	41.71331	244	59 536	15.62050	49.39636
36	1 296	6.000 000	18.97367	105	11 025	10.24695	32.40370	175	30 625	13.22876	41.83300	245	60 025	15.65248	49.49747
37	1 369	6.082 763	19.23538	106	11 236	10.29563	32.55764	176	30 976	13.26650	41.95235	246	60 516	15.68439	49.59839
38	1 444	6.164 414	19.49359	107	11 449	10.34408	32.71085	177	31 329	13.30413	42.07137	247	61 009	15.71623	49.69909
39	1 521	6.244 998	19.74842	108	11 664	10.39230	32.86335	178	31 684	13.34166	42.19005	248	61 504	15.74802	49.79960
40	1 600	6.324 555	20.00000	109	11 881	10.44031	33.01515	179	32 041	13.37909	42.30839	249	62 001	15.77973	49.89990
41	1 681	6.403 124	20.24846	110	12 100	10.48809	33.16625	180	32 400	13.41641	42.42641	250	62 500	15.81139	50.00000
42	1 764	6.480 741	20.49390	111	12 321	10.53565	33.31666	181	32 761	13.45362	42.54409	251	63 001	15.84298	50.09990
43	1 849	6.557 439	20.73644	112	12 544	10.58301	33.46640	182	33 124	13.49074	42.66146	252	63 504	15.87451	50.19960
44	1 936	6.633 250	20.97618	113	12 769	10.63015	33.61547	183	33 489	13.52775	42.77850	253	64 009	15.90597	50.29911
45	2 025	6.708 204	21.21320	114	12 996	10.67708	33.76389	184	33 856	13.56466	42.89522	254	64 516	15.93738	50.39841
46	2 116	6.782 330	21.44761	115	13 225	10.72381	33.91165	185	34 225	13.60147	43.01163	255	65 025	15.96872	50.49752
47	2 209	6.855 655	21.67948	116	13 456	10.77033	34.05877	186	34 596	13.63818	43.12772	256	65 536	16.00000	50.59644
48	2 304	6.928 203	21.90890	117	13 689	10.81665	34.20526	187	34 969	13.67479	43.24350	257	66 049	16.03122	50.69517
49	2 401	7.000 000	22.13594	118	13 924	10.86278	34.35113	188	35 344	13.71131	43.35897	258	66 564	16.06238	50.79370
50	2 500	7.071 068	22.36068	119	14 161	10.90871	34.49638	189	35 721	13.74773	43.47413	259	67 081	16.09348	50.89204
51	2 601	7.141 428	22.58318	120	14 400	10.95445	34.64102	190	36 100	13.78405	43.58899	260	67 600	16.12452	50.99020
52	2 704	7.211 103	22.80351	121	14 641	11.00000	34.78505	191	36 481	13.82027	43.70355	261	68 121	16.15549	51.08816
53	2 809	7.280 110	23.02173	122	14 884	11.04536	34.92850	192	36 864	13.85641	43.81780	262	68 644	16.18641	51.18594
54	2 916	7.348 469	23.23790	123	15 129	11.09054	35.07136	193	37 249	13.89244	43.93177	263	69 169	16.21727	51.28353
55	3 025	7.416 198	23.45208	124	15 376	11.13553	35.21363	194	37 636	13.92839	44.04543	264	69 696	16.24808	51.38093
56	3 136	7.483 315	23.66432	125	15 625	11.18034	35.35534	195	38 025	13.96424	44.15880	265	70 225	16.27882	51.47815
57	3 249	7.549 834	23.87467	126	15 876	11.22497	35.49648	196	38 416	14.00000	44.27189	266	70 756	16.30951	51.57519
58	3 364	7.615 773	24.08319	127	16 129	11.26943	35.63706	197	38 809	14.03567	44.38468	267	71 289	16.34013	51.67204
59	3 481	7.681 146	24.28992	128	16 384	11.31371	35.77709	198	39 204	14.07125	44.49719	268	71 824	16.37071	51.76872
60	3 600	7.745 967	24.49490	129	16 641	11.35782	35.91657	199	39 601	14.10674	44.60942	269	72 361	16.40122	51.86521
61	3 721	7.810 250	24.69818	130	16 900	11.40175	36.05551	200	40 000	14.14214	44.72136	270	72 900	16.43168	51.96152
62	3 844	7.874 008	24.89980	131	17 161	11.44552	36.19392	201	40 401	14.17745	44.83302	271	73 441	16.46208	52.05766
63	3 969	7.937 254	25.09980	132	17 424	11.48913	36.33180	202	40 804	14.21267	44.94441	272	73 984	16.49242	52.15362
64	4 096	8.000 000	25.29822	133	17 689	11.53256	36.46917	203	41 209	14.24781	45.05552	273	74 529	16.52271	52.24940
65	4 225	8.062 258	25.49510	134	17 956	11.57584	36.60601	204	41 616	14.28286	45.16636	274	75 076	16.55295	52.34501
66	4 356	8.124 038	25.69047	135	18 225	11.61895	36.74235	205	42 025	14.31782</					

n	n^2	\sqrt{n}	$\sqrt{10n}$	n	n^2	\sqrt{n}	$\sqrt{10n}$	n	n^2	\sqrt{n}	$\sqrt{10n}$	n	n^2	\sqrt{n}	$\sqrt{10n}$
280	78 400	16.73320	52.91503	355	126 025	18.84144	59.58188	430	184 900	20.73644	65.57439	505	255 025	22.47221	71.06335
281	78 961	16.76305	53.00943	356	126 736	18.86796	59.66574	431	185 761	20.76054	65.65059	506	256 036	22.49444	71.13368
282	79 524	16.79286	53.10367	357	127 449	18.89444	59.74948	432	186 624	20.78461	65.72671	507	257 049	22.51666	71.20393
283	80 089	16.82260	53.19774	358	128 164	18.92089	59.83310	433	187 489	20.80865	65.80274	508	258 064	22.53886	71.27412
284	80 656	16.85230	53.29165	359	128 881	18.94730	59.91661	434	188 356	20.83267	65.87868	509	259 081	22.56103	71.34424
285	81 225	16.88194	53.38539	360	129 600	18.97367	60.00000	435	189 225	20.85665	65.95453	510	260 100	22.58318	71.41438
286	81 796	16.91153	53.47897	361	130 321	19.00000	60.08328	436	190 096	20.88061	66.03030	511	261 121	22.60531	71.48452
287	82 369	16.94107	53.57238	362	131 044	19.02630	60.16644	437	190 969	20.90454	66.10598	512	262 144	22.62742	71.55418
288	82 944	16.97056	53.66563	363	131 769	19.05256	60.24948	438	191 844	20.92845	66.18157	513	263 169	22.64950	71.62402
289	83 521	17.00000	53.75872	364	132 496	19.07878	60.33241	439	192 721	20.95233	66.25708	514	264 196	22.67157	71.69379
290	84 100	17.02939	53.85165	365	133 225	19.10497	60.41523	440	193 600	20.97618	66.33250	515	265 225	22.69361	71.76350
291	84 681	17.05872	53.94442	366	133 956	19.13113	60.49793	441	194 481	21.00000	66.40783	516	266 256	22.71563	71.83314
292	85 264	17.08801	54.03702	367	134 689	19.15724	60.58052	442	195 364	21.02380	66.48308	517	267 289	22.73763	71.90277
293	85 849	17.11724	54.12947	368	135 424	19.18333	60.66300	443	196 249	21.04757	66.55825	518	268 324	22.75961	71.97222
294	86 436	17.14643	54.22177	369	136 161	19.20937	60.74537	444	197 136	21.07131	66.63332	519	269 361	22.78157	72.04165
295	87 025	17.17556	54.31390	370	136 900	19.23538	60.82763	445	198 025	21.09502	66.70832	520	270 400	22.80351	72.11103
296	87 616	17.20465	54.40588	371	137 641	19.26136	60.90977	446	198 916	21.11871	66.78323	521	271 441	22.82542	72.18033
297	88 209	17.23369	54.49771	372	138 384	19.28730	60.99180	447	199 809	21.14237	66.85806	522	272 484	22.84732	72.24957
298	88 804	17.26268	54.58938	373	139 129	19.31321	61.07373	448	200 704	21.16601	66.93280	523	273 529	22.86919	72.31874
299	89 401	17.29162	54.68089	374	139 876	19.33908	61.15554	449	201 601	21.18962	67.00746	524	274 576	22.89105	72.38784
300	90 000	17.32051	54.77226	375	140 625	19.36492	61.23724	450	202 500	21.21320	67.08204	525	275 625	22.91288	72.45688
301	90 601	17.34935	54.86347	376	141 376	19.39072	61.31884	451	203 401	21.23676	67.15653	526	276 676	22.93469	72.52586
302	91 204	17.37815	54.95453	377	142 129	19.41649	61.40033	452	204 304	21.26029	67.23095	527	277 729	22.95648	72.59477
303	91 809	17.40690	55.04544	378	142 884	19.44222	61.48170	453	205 209	21.28380	67.30527	528	278 784	22.97825	72.66361
304	92 416	17.43560	55.13620	379	143 641	19.46792	61.56298	454	206 116	21.30728	67.37952	529	279 841	23.00000	72.73239
305	93 025	17.46425	55.22681	380	144 400	19.49359	61.64414	455	207 025	21.33073	67.45369	530	280 900	23.02173	72.80110
306	93 636	17.49286	55.31727	381	145 161	19.51922	61.72520	456	207 936	21.35416	67.52777	531	281 961	23.04344	72.86975
307	94 249	17.52142	55.40758	382	145 924	19.54482	61.80615	457	208 849	21.37756	67.60178	532	283 024	23.06513	72.93833
308	94 864	17.54993	55.49775	383	146 689	19.57039	61.88699	458	209 764	21.40093	67.67570	533	284 089	23.08679	73.00685
309	95 481	17.57840	55.58777	384	147 456	19.59592	61.96773	459	210 681	21.42429	67.74954	534	285 156	23.10844	73.07530
310	96 100	17.60682	55.67764	385	148 225	19.62142	62.04837	460	211 600	21.44761	67.82330	535	286 225	23.13007	73.14369
311	96 721	17.63519	55.76737	386	148 996	19.64688	62.12890	461	212 521	21.47091	67.89698	536	287 296	23.15167	73.21202
312	97 344	17.66352	55.85696	387	149 769	19.67232	62.20932	462	213 444	21.49419	67.97058	537	288 369	23.17326	73.28028
313	97 969	17.69181	55.94640	388	150 544	19.69772	62.28965	463	214 369	21.51743	68.04410	538	289 444	23.19483	73.34848
314	98 596	17.72005	56.03570	389	151 321	19.72308	62.36986	464	215 296	21.54066	68.11755	539	290 521	23.21637	73.41662
315	99 225	17.74824	56.12486	390	152 100	19.74842	62.44998	465	216 225	21.56386	68.19091	540	291 600	23.23790	73.48469
316	99 856	17.77639	56.21388	391	152 881	19.77372	62.52999	466	217 156	21.58703	68.26419	541	292 681	23.25941	73.55270
317	100 489	17.80449	56.30275	392	153 664	19.79899	62.60990	467	218 089	21.61018	68.33740	542	293 764	23.28089	73.62065
318	101 124	17.83255	56.39149	393	154 449	19.82423	62.68971	468	219 024	21.63331	68.41053	543	294 849	23.30236	73.68853
319	101 761	17.86057	56.48008	394	155 236	19.84943	62.76942	469	219 961	21.65641	68.48357	544	295 936	23.32381	73.75636
320	102 400	17.88854	56.56854	395	156 025	19.87461	62.84903	470	220 900	21.67948	68.55655	545	297 025	23.34524	73.82412
321	103 041	17.91647	56.65686	396	156 816	19.89975	62.92853	471	221 841	21.70253	68.62944	546	298 116	23.36664	73.89181
322	103 684	17.94436	56.74504	397	157 609	19.92486	63.00794	472	222 784	21.72556	68.70226	547	299 209	23.38803	73.95945
323	104 329	17.97220	56.83309	398	158 404	19.94994	63.08724	473	223 729	21.74856	68.77500	548	300 304	23.40940	74.02702
324	104 976	18.00000	56.92100	399	159 201	19.97498	63.16645	474	224 676	21.77154	68.84766	549	301 401	23.43075	74.09453
325	105 625	18.02776	57.00877	400	160 000	20.00000	63.24555	475	225 625	21.79449	68.92024	550	302 500	23.45208	74.16198
326	106 276	18.05547	57.09641	401	160 801	20.02498	63.32456	476	226 576	21.81742	68.99275	551	303 601	23.47339	74.22937
327	106 929	18.08314	57.18391	402	161 604	20.04994	63.40347	477	227 529	21.84033	69.06519	552	304 704	23.49468	74.29670
328	107 584	18.11077	57.27128	403	162 409	20.07486	63.48228	478	228 484	21.86321	69.13754	553	305 809	23.51595	74.36397
329	108 241	18.13836	57.35852	404	163 216	20.09975	63.56099	479	229 441	21.88607	69.20983	554	306 916	23.53720	74.43118
330	108 900	18.16590	57.44563	405	164 025	20.12461	63.63961	480	230 400	21.90890	69.28203	555	308 025	23.55844	74.49832
331	109 561	18.19341	57.53260	406	164 836	20.14944	63.71813	481	231 361	21.93171	69.35416	556	309 136	23.57965	74.56541
332	110 224	18.22087	57.61944	407	165 649	20.17424	63.79655	482	232 324	21.95450	69.42622	557	310 249	23.60085	74.63243
333	110 889	18.24829	57.70615	408	166 464	20.19901	63.87488	483	233 289	21.97726	69.49820	558	311 364	23.62202	74.69940
334	111 556	18.27567	57.79273	409	167 281	20.22375	63.95311	484	234 256	22.00000	69.57011	559	312 481	23.64318	74.76630
335	112 225	18.30301	57.87918	410	168 100	20.24846	64.03124	485	235 225	22.02272	69.64194	560	313 600	23.66432	74.83315
336	112 896	18.33030	57.96551	411	168 921	20.27313	64.10928	486	236 196	22.04541	69.71370	561	314 721	23.68544	74.89993
337	113 569	18.35756	58.05170	412	169 744	20.29778	64.18723	487	237 169	22.06808	69.78539	562	315 844	23.70654	74.96666
338	114 244	18.38478	58.13777	413	170 569	20.32240	64.26508	488	238 144	22.09072	69.85700	563	316 969	23.72762	75.03333
339	114 921	18.41195	58.22371	414	171 396	20.34699	64.34283	489	239 121	22.11334	69.92853	564	318 096	23.74868	75.09993
340	115 600	18.43909	58.30952	415	172 225	20.37155	64.42049	490	240 100	22.13594	70.00000	565	319 225	23.76973	75.16648
341	116 281	18.46619	58.39521	416	173 056	20.39608	64.49806	491	241 081	22.15852	70.07139	566	320 356	23.79075	75.23297
342	116 964	18.49324	58.48077	417	173 889	20.42058	64.57554	492	242 064	22.18107	70.14271	567	321 489	23.81176	75.29940
343	117 649	18.52026	58.56620	418	174 724	20.44505	64.65292	493	243 049	22.20360	70.21396	568	322 624	23.83275	75.36577
344	118 336	18.54724	58.65151	419	175 561	20.46949	64.73021	494	244 036	22.22611	70.2				

	n^2	\sqrt{n}	$\sqrt{10n}$	n	n^2	\sqrt{n}	$\sqrt{10n}$	n	n^2	\sqrt{n}	$\sqrt{10n}$	n	n^2	\sqrt{n}	$\sqrt{10n}$
0	336 400	24.08319	76.15773	655	429 025	25.59297	80.93207	730	532 900	27.01851	85.44004	805	648 025	28.37252	89.72179
1	337 561	24.10394	76.22336	656	430 336	25.61250	80.99383	731	534 361	27.03701	85.49854	806	649 636	28.39014	89.77750
2	338 724	24.12468	76.28892	657	431 649	25.63201	81.05554	732	535 824	27.05550	85.55700	807	651 249	28.40775	89.83318
3	339 889	24.14539	76.35444	658	432 964	25.65151	81.11720	733	537 289	27.07397	85.61542	808	652 864	28.42534	89.88882
4	341 056	24.16609	76.41989	659	434 281	25.67100	81.17881	734	538 756	27.09243	85.67380	809	654 481	28.44293	89.94443
5	342 225	24.18677	76.48529	660	435 600	25.69047	81.24038	735	540 225	27.11088	85.73214	810	656 100	28.46050	90.00000
6	343 396	24.20744	76.55064	661	436 921	25.70992	81.30191	736	541 696	27.12932	85.79044	811	657 721	28.47806	90.05554
7	344 569	24.22808	76.61593	662	438 244	25.72936	81.36338	737	543 169	27.14774	85.84870	812	659 344	28.49561	90.11104
8	345 744	24.24871	76.68116	663	439 569	25.74879	81.42481	738	544 644	27.16616	85.90693	813	660 969	28.51315	90.16651
9	346 921	24.26932	76.74634	664	440 896	25.76820	81.48620	739	546 121	27.18455	85.96511	814	662 596	28.53069	90.22195
0	348 100	24.28992	76.81146	665	442 225	25.78759	81.54753	740	547 600	27.20294	86.02325	815	664 225	28.54820	90.27735
1	349 281	24.31049	76.87652	666	443 556	25.80698	81.60882	741	549 081	27.22132	86.08136	816	665 856	28.56571	90.33272
2	350 464	24.33105	76.94154	667	444 889	25.82634	81.67007	742	550 564	27.23968	86.13942	817	667 489	28.58321	90.38805
3	351 649	24.35159	77.00649	668	446 224	25.84570	81.73127	743	552 049	27.25803	86.19745	818	669 124	28.60070	90.44335
4	352 836	24.37212	77.07140	669	447 561	25.86503	81.79242	744	553 536	27.27636	86.25543	819	670 761	28.61818	90.49862
5	354 025	24.39262	77.13624	670	448 900	25.88436	81.85353	745	555 025	27.29469	86.31338	820	672 400	28.63564	90.55385
6	355 216	24.41311	77.20104	671	450 241	25.90367	81.91459	746	556 516	27.31300	86.37129	821	674 041	28.65310	90.60905
7	356 409	24.43358	77.26578	672	451 584	25.92296	81.97561	747	558 009	27.33130	86.42916	822	675 684	28.67054	90.66422
8	357 604	24.45404	77.33046	673	452 929	25.94224	82.03658	748	559 504	27.34959	86.48699	823	677 329	28.68798	90.71935
9	358 801	24.47448	77.39509	674	454 276	25.96151	82.09750	749	561 001	27.36786	86.54479	824	678 976	28.70540	90.77445
0	360 000	24.49490	77.45967	675	455 625	25.98076	82.15838	750	562 500	27.38613	86.60254	825	680 625	28.72281	90.82951
1	361 201	24.51530	77.52419	676	456 976	26.00000	82.21922	751	564 001	27.40438	86.66026	826	682 276	28.74022	90.88454
2	362 404	24.53569	77.58866	677	458 329	26.01922	82.28001	752	565 504	27.42262	86.71793	827	683 929	28.75761	90.93954
3	363 609	24.55606	77.65307	678	459 684	26.03843	82.34076	753	567 009	27.44085	86.77557	828	685 584	28.77499	90.99451
4	364 816	24.57641	77.71744	679	461 041	26.05763	82.40146	754	568 516	27.45906	86.83317	829	687 241	28.79236	91.04944
5	366 025	24.59675	77.78175	680	462 400	26.07681	82.46211	755	570 025	27.47726	86.89074	830	688 900	28.80972	91.10434
6	367 236	24.61707	77.84600	681	463 761	26.09598	82.52272	756	571 536	27.49545	86.94826	831	690 561	28.82707	91.15920
7	368 449	24.63737	77.91020	682	465 124	26.11513	82.58329	757	573 049	27.51363	87.00575	832	692 224	28.84441	91.21403
8	369 664	24.65766	77.97435	683	466 489	26.13427	82.64381	758	574 564	27.53180	87.06320	833	693 889	28.86174	91.26883
9	370 881	24.67793	78.03845	684	467 856	26.15339	82.70429	759	576 081	27.54995	87.12061	834	695 556	28.87906	91.32360
0	372 100	24.69818	78.10250	685	469 225	26.17250	82.76473	760	577 600	27.56810	87.17798	835	697 225	28.89637	91.37833
1	373 321	24.71841	78.16649	686	470 596	26.19160	82.82512	761	579 121	27.58623	87.23531	836	698 896	28.91366	91.43304
2	374 544	24.73863	78.23043	687	471 969	26.21068	82.88546	762	580 644	27.60435	87.29261	837	700 569	28.93095	91.48770
3	375 769	24.75884	78.29432	688	473 344	26.22975	82.94577	763	582 169	27.62245	87.34987	838	702 244	28.94823	91.54234
4	376 996	24.77902	78.35815	689	474 721	26.24881	83.00602	764	583 696	27.64055	87.40709	839	703 921	28.96550	91.59694
5	378 225	24.79919	78.42194	690	476 100	26.26785	83.06624	765	585 225	27.65863	87.46428	840	705 600	28.98275	91.65151
6	379 456	24.81935	78.48567	691	477 481	26.28688	83.12641	766	586 756	27.67671	87.52143	841	707 281	29.00000	91.70605
7	380 689	24.83948	78.54935	692	478 864	26.30589	83.18654	767	588 289	27.69476	87.57854	842	708 964	29.01724	91.76056
8	381 924	24.85961	78.61298	693	480 249	26.32489	83.24662	768	589 824	27.71281	87.63561	843	710 649	29.03446	91.81503
9	383 161	24.87971	78.67655	694	481 636	26.34388	83.30666	769	591 361	27.73085	87.69265	844	712 336	29.05168	91.86947
0	384 400	24.89980	78.74008	695	483 025	26.36285	83.36666	770	592 900	27.74887	87.74964	845	714 025	29.06888	91.92388
1	385 641	24.91987	78.80355	696	484 416	26.38181	83.42661	771	594 441	27.76689	87.80661	846	715 716	29.08608	91.97826
2	386 884	24.93993	78.86698	697	485 809	26.40076	83.48653	772	595 984	27.78489	87.86353	847	717 409	29.10326	92.03260
3	388 129	24.95997	78.93035	698	487 204	26.41969	83.54639	773	597 529	27.80288	87.92042	848	719 104	29.12044	92.08692
4	389 376	24.97999	78.99367	699	488 601	26.43861	83.60622	774	599 076	27.82086	87.97727	849	720 801	29.13760	92.14120
5	390 625	25.00000	79.05694	700	490 000	26.45751	83.66600	775	600 625	27.83882	88.03408	850	722 500	29.15476	92.19544
6	391 876	25.01999	79.12016	701	491 401	26.47640	83.72574	776	602 176	27.85678	88.09086	851	724 201	29.17190	92.24966
7	393 129	25.03997	79.18333	702	492 804	26.49528	83.78544	777	603 729	27.87472	88.14760	852	725 904	29.18904	92.30385
8	394 384	25.05993	79.24645	703	494 209	26.51415	83.84510	778	605 284	27.89265	88.20431	853	727 609	29.20616	92.35800
9	395 641	25.07987	79.30952	704	495 616	26.53300	83.90471	779	606 841	27.91057	88.26098	854	729 316	29.22328	92.41212
0	396 900	25.09980	79.37254	705	497 025	26.55184	83.96428	780	608 400	27.92848	88.31761	855	731 025	29.24038	92.46621
1	398 161	25.11971	79.43551	706	498 436	26.57066	84.02381	781	609 961	27.94638	88.37420	856	732 736	29.25748	92.52027
2	399 424	25.13961	79.49843	707	499 849	26.58947	84.08329	782	611 524	27.96426	88.43076	857	734 449	29.27456	92.57429
3	400 689	25.15949	79.56130	708	501 264	26.60827	84.14274	783	613 089	27.98214	88.48729	858	736 164	29.29164	92.62829
4	401 956	25.17936	79.62412	709	502 681	26.62705	84.20214	784	614 656	28.00000	88.54377	859	737 881	29.30870	92.68225
5	403 225	25.19921	79.68689	710	504 100	26.64583	84.26150	785	616 225	28.01785	88.60023	860	739 600	29.32576	92.73618
6	404 496	25.21904	79.74961	711	505 521	26.66458	84.32082	786	617 796	28.03569	88.65664	861	741 321	29.34280	92.79009
7	405 769	25.23886	79.81228	712	506 944	26.68333	84.38009	787	619 369	28.05352	88.71302	862	743 044	29.35984	92.84396
8	407 044	25.25866	79.87490	713	508 369	26.70206	84.43933	788	620 944	28.07134	88.76936	863	744 769	29.37686	92.89779
9	408 321	25.27845	79.93748	714	509 796	26.72078	84.49852	789	622 521	28.08914	88.82567	864	746 496	29.39388	92.95160
0	409 600	25.29822	80.00000	715	511 225	26.73948	84.55767	790	624 100	28.10694	88.88194	865	748 225	29.41088	93.00538
1	410 881	25.31798	80.06248	716	512 656	26.75818	84.61678	791	625 681	28.12472	88.93818	866	749 956	29.42788	93.05912
2	412 164	25.33772	80.12490	717	514 089	26.77686	84.67585	792	627 264	28.14249	88.99438	867	751 689	29.44486	93.11283
3	413 449	25.35744	80.18728	718	515 524	26.79552	84.73488	793	628 849	28.16026	89.05055	868	753 424	29.46184	93.16652
4	414 736	25.37716	80.24961	719	516 961	26.81418	84.79387	794	630 436	28.17801	89.10668	869	755 161	29.47881	93.22017
5	416 0														

<i>n</i>	<i>n</i> ²	\sqrt{n}	$\sqrt{10n}$	<i>n</i>	<i>n</i> ²	\sqrt{n}	$\sqrt{10n}$	<i>n</i>	<i>n</i> ²	\sqrt{n}	$\sqrt{10n}$	<i>n</i>	<i>n</i> ²	\sqrt{n}	$\sqrt{10n}$
880	774 400	29.66479	93.80832	910	828 100	30.16621	95.39392	940	883 600	30.65942	96.95360	970	940 900	31.14482	98.48858
881	776 161	29.68164	93.86160	911	829 921	30.18278	95.44632	941	885 481	30.67572	97.00515	971	942 841	31.16087	98.53933
882	777 924	29.69848	93.91486	912	831 744	30.19934	95.49869	942	887 364	30.69202	97.05668	972	944 784	31.17691	98.59000
883	779 689	29.71532	93.96808	913	833 569	30.21589	95.55103	943	889 249	30.70831	97.10819	973	946 729	31.19295	98.64076
884	781 456	29.73214	94.02127	914	835 396	30.23243	95.60335	944	891 136	30.72458	97.15966	974	948 676	31.20897	98.69144
885	783 225	29.74895	94.07444	915	837 225	30.24897	95.65563	945	893 025	30.74085	97.21111	975	950 625	31.22499	98.74201
886	784 996	29.76575	94.12757	916	839 056	30.26549	95.70789	946	894 916	30.75711	97.26253	976	952 576	31.24100	98.79273
887	786 769	29.78255	94.18068	917	840 889	30.28201	95.76012	947	896 809	30.77337	97.31393	977	954 529	31.25700	98.84331
888	788 544	29.79933	94.23375	918	842 724	30.29851	95.81232	948	898 704	30.78961	97.36529	978	956 484	31.27299	98.89388
889	790 321	29.81610	94.28680	919	844 561	30.31501	95.86449	949	900 601	30.80584	97.41663	979	958 441	31.28898	98.94443
890	792 100	29.83287	94.33981	920	846 400	30.33150	95.91663	950	902 500	30.82207	97.46794	980	960 400	31.30495	98.99499
891	793 881	29.84962	94.39280	921	848 241	30.34798	95.96874	951	904 401	30.83829	97.51923	981	962 361	31.32092	99.04544
892	795 664	29.86637	94.44575	922	850 084	30.36445	96.02083	952	906 304	30.85450	97.57049	982	964 324	31.33688	99.09591
893	797 449	29.88311	94.49868	923	851 929	30.38092	96.07289	953	908 209	30.87070	97.62172	983	966 289	31.35283	99.14636
894	799 236	29.89983	94.55157	924	853 776	30.39737	96.12492	954	910 116	30.88689	97.67292	984	968 256	31.36877	99.19677
895	801 025	29.91655	94.60444	925	855 625	30.41381	96.17692	955	912 025	30.90307	97.72410	985	970 225	31.38471	99.24717
896	802 816	29.93326	94.65728	926	857 476	30.43025	96.22889	956	913 936	30.91925	97.77525	986	972 196	31.40064	99.29753
897	804 609	29.94996	94.71008	927	859 329	30.44667	96.28084	957	915 849	30.93542	97.82638	987	974 169	31.41656	99.34787
898	806 404	29.96665	94.76286	928	861 184	30.46309	96.33276	958	917 764	30.95158	97.87747	988	976 144	31.43247	99.39819
899	808 201	29.98333	94.81561	929	863 041	30.47950	96.38465	959	919 681	30.96773	97.92855	989	978 121	31.44837	99.44848
900	810 000	30.00000	94.86833	930	864 900	30.49590	96.43651	960	921 600	30.98387	97.97959	990	980 100	31.46427	99.49874
901	811 801	30.01666	94.92102	931	866 761	30.51229	96.48834	961	923 521	31.00000	98.03061	991	982 081	31.48015	99.54881
902	813 604	30.03331	94.97368	932	868 624	30.52868	96.54015	962	925 444	31 01612	98.08160	992	984 064	31.49603	99.59920
903	815 409	30.04996	95.02631	933	870 489	30.54505	96.59193	963	927 369	31.03224	98.13256	993	986 049	31.51190	99.64939
904	817 216	30.06659	95.07891	934	872 356	30.56141	96.64368	964	929 296	31.04835	98.18350	994	988 036	31.52777	99.69955
905	819 025	30.08322	95.13149	935	874 225	30.57777	96.69540	965	931 225	31.06445	98.23441	995	990 025	31.54362	99.74969
906	820 836	30.09983	95.18403	936	876 096	30.59412	96.74709	966	933 156	31.08054	98.28530	996	992 016	31.55947	99.79980
907	822 649	30.11644	95.23655	937	877 969	30.61046	96.79876	967	935 089	31.09662	98.33616	997	994 009	31.57531	99.84989
908	824 464	30.13304	95.28903	938	879 844	30.62679	96.85040	968	937 024	31.11270	98.38699	998	996 004	31.59114	99.89995
909	826 281	30.14963	95.34149	939	881 721	30.64311	96.90201	969	938 961	31.12876	98.43780	999	998 001	31.60696	99.94999

Factorials* and their Logarithms

<i>n</i>	<i>n</i> !	log ₁₀ <i>n</i> !	<i>n</i>	<i>n</i> !	log ₁₀ <i>n</i> !	<i>n</i>	<i>n</i> !	log ₁₀ <i>n</i> !
1	1.0000	0.00000	35	1.0333 × 10 ⁴⁰	40.01423	70	1.1979 × 10 ¹⁰⁰	100.07841
2	2.0000	0.30103	36	3.7199 × 10 ⁴¹	41.57054	71	8.5048 × 10 ¹⁰¹	101.92966
3	6.0000	0.77815	37	1.3764 × 10 ⁴³	43.13874	72	6.1234 × 10 ¹⁰³	103.78700
4	2.4000 × 10	1.38021	38	5.2302 × 10 ⁴⁴	44.71852	73	4.4701 × 10 ¹⁰⁵	105.65032
5	1.2000 × 10 ³	2.07918	39	2.0398 × 10 ⁴⁶	46.30959	74	3.3079 × 10 ¹⁰⁷	107.51955
6	7.2000 × 10 ³	2.85733	40	8.1592 × 10 ⁴⁷	47.91165	75	2.4809 × 10 ¹⁰⁹	109.39461
7	5.0400 × 10 ³	3.70243	41	3.3453 × 10 ⁴⁹	49.52443	76	1.8855 × 10 ¹¹¹	111.27543
8	4.0320 × 10 ⁴	4.60552	42	1.4050 × 10 ⁵¹	51.14768	77	1.4518 × 10 ¹¹³	113.16192
9	3.6288 × 10 ⁵	5.55976	43	6.0415 × 10 ⁵²	52.78115	78	1.1324 × 10 ¹¹⁵	115.05401
10	3.6288 × 10 ⁶	6.55976	44	2.6583 × 10 ⁵⁴	54.42460	79	8.9462 × 10 ¹¹⁶	116.95164
11	3.9917 × 10 ⁷	7.60116	45	1.1962 × 10 ⁵⁶	56.07781	80	7.1569 × 10 ¹¹⁸	118.85473
12	4.7900 × 10 ⁸	8.68034	46	5.5026 × 10 ⁵⁷	57.74057	81	5.7971 × 10 ¹²⁰	120.76321
13	6.2270 × 10 ⁹	9.79428	47	2.5862 × 10 ⁵⁹	59.41267	82	4.7536 × 10 ¹²²	122.67703
14	8.7178 × 10 ¹⁰	10.94041	48	1.2414 × 10 ⁶¹	61.09391	83	3.9455 × 10 ¹²⁴	124.59610
15	1.3077 × 10 ¹²	12.11650	49	6.0828 × 10 ⁶²	62.78410	84	3.3142 × 10 ¹²⁶	126.52038
16	2.0923 × 10 ¹³	13.32062	50	3.0414 × 10 ⁶⁴	64.48307	85	2.8171 × 10 ¹²⁸	128.44980
17	3.5569 × 10 ¹⁴	14.55107	51	1.5511 × 10 ⁶⁶	66.19065	86	2.4227 × 10 ¹³⁰	130.38430
18	6.4024 × 10 ¹⁵	15.80634	52	8.0658 × 10 ⁶⁷	67.90665	87	2.1078 × 10 ¹³²	132.32382
19	1.2165 × 10 ¹⁷	17.08509	53	4.2749 × 10 ⁶⁹	69.63092	88	1.8548 × 10 ¹³⁴	134.26830
20	2.4329 × 10 ¹⁸	18.38612	54	2.3084 × 10 ⁷¹	71.36332	89	1.6508 × 10 ¹³⁶	136.21769
21	5.1091 × 10 ¹⁹	19.70834	55	1.2696 × 10 ⁷³	73.10368	90	1.4857 × 10 ¹³⁸	138.17194
22	1.1240 × 10 ²¹	21.05077	56	7.1100 × 10 ⁷⁴	74.85187	91	1.3520 × 10 ¹⁴⁰	140.13098
23	2.5852 × 10 ²²	22.41249	57	4.0527 × 10 ⁷⁶	76.60774	92	1.2438 × 10 ¹⁴²	142.09477
24	6.2045 × 10 ²³	23.79271	58	2.3506 × 10 ⁷⁸	78.37117	93	1.1568 × 10 ¹⁴⁴	144.06325
25	1.5511 × 10 ²⁵	25.19065	59	1.3868 × 10 ⁸⁰	80.14202	94	1.0874 × 10 ¹⁴⁶	146.03638
26	4.0329 × 10 ²⁶	26.60562	60	8.3210 × 10 ⁸¹	81.92017	95	1.0330 × 10 ¹⁴⁸	148.01410
27	1.0889 × 10 ²⁸	28.03698	61	5.0758 × 10 ⁸³	83.70550	96	9.9168 × 10 ¹⁴⁹	149.99637
28	3.0489 × 10 ²⁹	29.48414	62	3.1470 × 10 ⁸⁵	85.49790	97	9.6193 × 10 ¹⁵¹	151.98314
29	8.8418 × 10 ³⁰	30.94654	63	1.9826 × 10 ⁸⁷	87.29724	98	9.4269 × 10 ¹⁵³	153.97437
30	2.6525 × 10 ³²	32.42366	64	1.2689 × 10 ⁸⁹	89.10342	99	9.3326 × 10 ¹⁵⁵	155.97000
31	8.2228 × 10 ³³	33.91502	65	8.2477 × 10 ⁹⁰	90.91633	100	9.3326 × 10 ¹⁵⁷	157.97000
32	2.6313 × 10 ³⁵	35.42017	66	5.4435 × 10 ⁹²	92.73587			
33	8.6833 × 10 ³⁶	36.93869	67	3.6471 × 10 ⁹⁴	94.56195			
34	2.9523 × 10 ³⁸	38.47016	68	2.4800 × 10 ⁹⁶	96.39446			
			69	1.7112 × 10 ⁹⁸	98.23331			

* *n*! = 1 × 2 × 3 × ... × (*n* − 1) × *n*

The following table gives the values of the area $\Phi(\epsilon)$ under the distribution from the ordinate at $\epsilon = 0$ to the ordinate for the value of ϵ given, as well as the corresponding ordinates $\varphi(\epsilon)$. These values and those given in the following tables of normal distribution are derived from the function:

$$\varphi(\epsilon) = \frac{1}{\sigma \sqrt{2\pi}} e^{-\epsilon^2/2\sigma^2}$$

where σ = standard deviation = 1, and e = base of natural logarithms.

ϵ	Areas $\Phi(\epsilon)$	Ordinates $\varphi(\epsilon)$	ϵ	Areas $\Phi(\epsilon)$	Ordinates $\varphi(\epsilon)$	ϵ	Areas $\Phi(\epsilon)$	Ordinates $\varphi(\epsilon)$	ϵ	Areas $\Phi(\epsilon)$	Ordinates $\varphi(\epsilon)$	ϵ	Areas $\Phi(\epsilon)$	Ordinates $\varphi(\epsilon)$	ϵ	Areas $\Phi(\epsilon)$	Ordinates $\varphi(\epsilon)$	ϵ	Areas $\Phi(\epsilon)$	Ordinates $\varphi(\epsilon)$
.00	.0000	.3989	.75	.2734	.3011	1.50	.4332	.1295	2.25	.4878	.0317	3.00	.4987	.0044	3.75	.4999	.0004	4.50	.5000	.0000
.01	.0040	.3989	.76	.2764	.2989	1.51	.4345	.1276	2.26	.4881	.0310	3.01	.4987	.0043	3.76	.4999	.0003	4.51	.5000	.0000
.02	.0080	.3989	.77	.2794	.2966	1.52	.4357	.1257	2.27	.4884	.0303	3.02	.4987	.0042	3.77	.4999	.0003	4.52	.5000	.0000
.03	.0120	.3988	.78	.2823	.2943	1.53	.4370	.1238	2.28	.4887	.0297	3.03	.4988	.0041	3.78	.4999	.0003	4.53	.5000	.0000
.04	.0160	.3986	.79	.2852	.2920	1.54	.4382	.1219	2.29	.4890	.0290	3.04	.4988	.0039	3.79	.4999	.0003	4.54	.5000	.0000
.05	.0199	.3984	.80	.2881	.2897	1.55	.4394	.1200	2.30	.4893	.0283	3.05	.4989	.0038	3.80	.4999	.0003	4.55	.5000	.0000
.06	.0239	.3982	.81	.2910	.2874	1.56	.4406	.1182	2.31	.4896	.0277	3.06	.4989	.0037	3.81	.4999	.0003	4.56	.5000	.0000
.07	.0279	.3980	.82	.2939	.2850	1.57	.4418	.1163	2.32	.4898	.0271	3.07	.4989	.0036	3.82	.4999	.0003	4.57	.5000	.0000
.08	.0319	.3977	.83	.2967	.2827	1.58	.4430	.1145	2.33	.4901	.0264	3.08	.4990	.0035	3.83	.4999	.0003	4.58	.5000	.0000
.09	.0359	.3973	.84	.2996	.2803	1.59	.4441	.1127	2.34	.4904	.0258	3.09	.4990	.0034	3.84	.4999	.0003	4.59	.5000	.0000
.10	.0398	.3970	.85	.3023	.2780	1.60	.4452	.1109	2.35	.4906	.0252	3.10	.4990	.0033	3.85	.4999	.0002	4.60	.5000	.0000
.11	.0438	.3965	.86	.3051	.2756	1.61	.4463	.1092	2.36	.4909	.0246	3.11	.4991	.0032	3.86	.4999	.0002	4.61	.5000	.0000
.12	.0478	.3961	.87	.3079	.2732	1.62	.4474	.1074	2.37	.4911	.0241	3.12	.4991	.0031	3.87	.5000	.0002	4.62	.5000	.0000
.13	.0517	.3956	.88	.3106	.2709	1.63	.4485	.1057	2.38	.4913	.0235	3.13	.4991	.0030	3.88	.5000	.0002	4.63	.5000	.0000
.14	.0557	.3951	.89	.3133	.2685	1.64	.4495	.1040	2.39	.4916	.0229	3.14	.4992	.0029	3.89	.5000	.0002	4.64	.5000	.0000
.15	.0596	.3945	.90	.3159	.2661	1.65	.4505	.1023	2.40	.4918	.0224	3.15	.4992	.0028	3.90	.5000	.0002	4.65	.5000	.0000
.16	.0636	.3939	.91	.3186	.2637	1.66	.4515	.1006	2.41	.4920	.0219	3.16	.4992	.0027	3.91	.5000	.0002	4.66	.5000	.0000
.17	.0675	.3932	.92	.3212	.2613	1.67	.4525	.0989	2.42	.4922	.0213	3.17	.4992	.0026	3.92	.5000	.0002	4.67	.5000	.0000
.18	.0714	.3925	.93	.3238	.2589	1.68	.4535	.0973	2.43	.4925	.0208	3.18	.4993	.0025	3.93	.5000	.0002	4.68	.5000	.0000
.19	.0754	.3918	.94	.3264	.2565	1.69	.4545	.0957	2.44	.4927	.0203	3.19	.4993	.0025	3.94	.5000	.0002	4.69	.5000	.0000
.20	.0793	.3910	.95	.3289	.2541	1.70	.4554	.0941	2.45	.4929	.0198	3.20	.4993	.0024	3.95	.5000	.0002	4.70	.5000	.0000
.21	.0832	.3902	.96	.3315	.2516	1.71	.4564	.0925	2.46	.4931	.0194	3.21	.4993	.0023	3.96	.5000	.0002	4.71	.5000	.0000
.22	.0871	.3894	.97	.3340	.2492	1.72	.4573	.0909	2.47	.4932	.0189	3.22	.4994	.0022	3.97	.5000	.0002	4.72	.5000	.0000
.23	.0910	.3885	.98	.3365	.2468	1.73	.4582	.0893	2.48	.4934	.0184	3.23	.4994	.0022	3.98	.5000	.0001	4.73	.5000	.0000
.24	.0948	.3876	.99	.3389	.2444	1.74	.4591	.0878	2.49	.4936	.0180	3.24	.4994	.0021	3.99	.5000	.0001	4.74	.5000	.0000
.25	.0987	.3867	1.00	.3413	.2420	1.75	.4599	.0863	2.50	.4938	.0175	3.25	.4994	.0020	4.00	.5000	.0001	4.75	.5000	.0000
.26	.1026	.3857	1.01	.3438	.2396	1.76	.4608	.0848	2.51	.4940	.0171	3.26	.4994	.0020	4.01	.5000	.0001	4.76	.5000	.0000
.27	.1064	.3847	1.02	.3461	.2371	1.77	.4616	.0833	2.52	.4941	.0167	3.27	.4995	.0019	4.02	.5000	.0001	4.77	.5000	.0000
.28	.1103	.3836	1.03	.3485	.2347	1.78	.4625	.0818	2.53	.4943	.0163	3.28	.4995	.0018	4.03	.5000	.0001	4.78	.5000	.0000
.29	.1141	.3825	1.04	.3508	.2323	1.79	.4633	.0804	2.54	.4945	.0159	3.29	.4995	.0018	4.04	.5000	.0001	4.79	.5000	.0000
.30	.1179	.3814	1.05	.3531	.2299	1.80	.4641	.0790	2.55	.4946	.0155	3.30	.4995	.0017	4.05	.5000	.0001	4.80	.5000	.0000
.31	.1217	.3802	1.06	.3554	.2275	1.81	.4649	.0775	2.56	.4948	.0151	3.31	.4995	.0017	4.06	.5000	.0001	4.81	.5000	.0000
.32	.1255	.3790	1.07	.3577	.2251	1.82	.4656	.0761	2.57	.4949	.0147	3.32	.4996	.0016	4.07	.5000	.0001	4.82	.5000	.0000
.33	.1293	.3778	1.08	.3599	.2227	1.83	.4664	.0748	2.58	.4951	.0143	3.33	.4996	.0016	4.08	.5000	.0001	4.83	.5000	.0000
.34	.1331	.3765	1.09	.3621	.2203	1.84	.4671	.0734	2.59	.4952	.0139	3.34	.4996	.0015	4.09	.5000	.0001	4.84	.5000	.0000
.35	.1368	.3752	1.10	.3643	.2179	1.85	.4678	.0721	2.60	.4953	.0136	3.35	.4996	.0015	4.10	.5000	.0001	4.85	.5000	.0000
.36	.1406	.3739	1.11	.3665	.2155	1.86	.4686	.0707	2.61	.4955	.0132	3.36	.4996	.0014	4.11	.5000	.0001	4.86	.5000	.0000
.37	.1443	.3726	1.12	.3686	.2131	1.87	.4693	.0694	2.62	.4956	.0129	3.37	.4996	.0014	4.12	.5000	.0001	4.87	.5000	.0000
.38	.1480	.3712	1.13	.3708	.2107	1.88	.4700	.0681	2.63	.4957	.0126	3.38	.4996	.0013	4.13	.5000	.0001	4.88	.5000	.0000
.39	.1517	.3697	1.14	.3729	.2083	1.89	.4706	.0669	2.64	.4959	.0122	3.39	.4997	.0013	4.14	.5000	.0001	4.89	.5000	.0000
.40	.1554	.3683	1.15	.3749	.2059	1.90	.4713	.0656	2.65	.4960	.0119	3.40	.4997	.0012	4.15	.5000	.0001	4.90	.5000	.0000
.41	.1591	.3668	1.16	.3770	.2036	1.91	.4719	.0644	2.66	.4961	.0116	3.41	.4997	.0012	4.16	.5000	.0001	4.91	.5000	.0000
.42	.1628	.3653	1.17	.3790	.2012	1.92	.4726	.0632	2.67	.4962	.0113	3.42	.4997	.0012	4.17	.5000	.0001	4.92	.5000	.0000
.43	.1664	.3637	1.18	.3810	.1989	1.93	.4732	.0620	2.68	.4963	.0110	3.43	.4997	.0011	4.18	.5000	.0001	4.93	.5000	.0000
.44	.1700	.3621	1.19	.3830	.1965	1.94	.4738	.0608	2.69	.4964	.0107	3.44	.4997	.0011	4.19	.5000	.0001	4.94	.5000	.0000
.45	.1736	.3605	1.20	.3849	.1942															

The Normal Distribution — Probit Transformation*

(Transformation of the sigmoid curve into a straight line by transformation of percentages into probits)

The percentages correspond to 100 times the area under the normal distribution between the ordinates $c = -\infty$ and c , the probits to the deviations c plus 5.

% → ↓	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1	2	3	4	5
	Probits														
0	...	1.9098	2.1218	2.2522	2.3479	2.4242	2.4879	2.5427	2.5911	2.6344					
1	2.6737	2.7096	2.7429	2.7738	2.8027	2.8299	2.8556	2.8799	2.9031	2.9251					
2	2.9463	2.9665	2.9859	3.0046	3.0226	3.0400	3.0569	3.0732	3.0890	3.1043					
3	3.1192	3.1337	3.1478	3.1616	3.1750	3.1881	3.2009	3.2134	3.2256	3.2376					
4	3.2493	3.2608	3.2721	3.2831	3.2940	3.3046	3.3151	3.3253	3.3354	3.3454					
5	3.3551	3.3648	3.3742	3.3836	3.3928	3.4018	3.4107	3.4195	3.4282	3.4368	9	18	27	36	45
6	3.4452	3.4536	3.4618	3.4699	3.4780	3.4859	3.4937	3.5015	3.5091	3.5167	8	16	24	32	40
7	3.5242	3.5316	3.5389	3.5462	3.5534	3.5605	3.5675	3.5745	3.5813	3.5882	7	14	21	28	36
8	3.5949	3.6016	3.6083	3.6148	3.6213	3.6278	3.6342	3.6405	3.6468	3.6531	6	13	19	26	32
9	3.6592	3.6654	3.6715	3.6775	3.6835	3.6894	3.6953	3.7012	3.7070	3.7127	6	12	18	24	30
10	3.7184	3.7241	3.7298	3.7354	3.7409	3.7464	3.7519	3.7574	3.7628	3.7681	6	11	17	22	28
11	3.7735	3.7788	3.7840	3.7893	3.7945	3.7996	3.8048	3.8099	3.8150	3.8200	5	10	16	21	26
12	3.8250	3.8300	3.8350	3.8399	3.8448	3.8497	3.8545	3.8593	3.8641	3.8689	5	10	15	20	24
13	3.8736	3.8783	3.8830	3.8877	3.8923	3.8969	3.9015	3.9061	3.9107	3.9152	5	9	14	18	23
14	3.9197	3.9242	3.9286	3.9331	3.9375	3.9419	3.9463	3.9506	3.9550	3.9593	4	9	13	18	22
15	3.9636	3.9678	3.9721	3.9763	3.9806	3.9848	3.9890	3.9931	3.9973	4.0014	4	8	13	17	21
16	4.0055	4.0096	4.0137	4.0178	4.0218	4.0259	4.0299	4.0339	4.0379	4.0419	4	8	12	16	20
17	4.0458	4.0498	4.0537	4.0576	4.0615	4.0654	4.0693	4.0731	4.0770	4.0808	4	8	12	16	19
18	4.0846	4.0884	4.0922	4.0960	4.0998	4.1035	4.1073	4.1110	4.1147	4.1184	4	8	11	15	19
19	4.1221	4.1258	4.1295	4.1331	4.1367	4.1404	4.1440	4.1476	4.1512	4.1548	4	7	11	15	18
20	4.1584	4.1619	4.1655	4.1690	4.1726	4.1761	4.1796	4.1831	4.1866	4.1901	4	7	11	14	18
21	4.1936	4.1970	4.2005	4.2039	4.2074	4.2108	4.2142	4.2176	4.2210	4.2244	3	7	10	14	17
22	4.2278	4.2312	4.2345	4.2379	4.2412	4.2446	4.2479	4.2512	4.2546	4.2579	3	7	10	13	17
23	4.2612	4.2644	4.2677	4.2710	4.2743	4.2775	4.2808	4.2840	4.2872	4.2905	3	7	10	13	16
24	4.2937	4.2969	4.3001	4.3033	4.3065	4.3097	4.3129	4.3160	4.3192	4.3224	3	6	10	13	16
25	4.3255	4.3287	4.3318	4.3349	4.3380	4.3412	4.3443	4.3474	4.3505	4.3536	3	6	9	12	16
26	4.3567	4.3597	4.3628	4.3659	4.3689	4.3720	4.3750	4.3781	4.3811	4.3842	3	6	9	12	15
27	4.3872	4.3902	4.3932	4.3962	4.3992	4.4022	4.4052	4.4082	4.4112	4.4142	3	6	9	12	15
28	4.4172	4.4201	4.4231	4.4260	4.4290	4.4319	4.4349	4.4378	4.4408	4.4437	3	6	9	12	15
29	4.4466	4.4495	4.4524	4.4554	4.4583	4.4612	4.4641	4.4670	4.4698	4.4727	3	6	9	12	14
30	4.4756	4.4785	4.4813	4.4842	4.4871	4.4899	4.4928	4.4956	4.4985	4.5013	3	6	9	11	14
31	4.5041	4.5070	4.5098	4.5126	4.5155	4.5183	4.5211	4.5239	4.5267	4.5295	3	6	8	11	14
32	4.5323	4.5351	4.5379	4.5407	4.5435	4.5462	4.5490	4.5518	4.5546	4.5573	3	6	8	11	14
33	4.5601	4.5628	4.5656	4.5684	4.5711	4.5739	4.5766	4.5793	4.5821	4.5848	3	5	8	11	14
34	4.5875	4.5903	4.5930	4.5957	4.5984	4.6011	4.6039	4.6066	4.6093	4.6120	3	5	8	11	14
35	4.6147	4.6174	4.6201	4.6228	4.6255	4.6281	4.6308	4.6335	4.6362	4.6389	3	5	8	11	13
36	4.6415	4.6442	4.6469	4.6495	4.6522	4.6549	4.6575	4.6602	4.6628	4.6655	3	5	8	11	13
37	4.6681	4.6708	4.6734	4.6761	4.6787	4.6814	4.6840	4.6866	4.6893	4.6919	3	5	8	11	13
38	4.6945	4.6971	4.6998	4.7024	4.7050	4.7076	4.7102	4.7129	4.7155	4.7181	3	5	8	10	13
39	4.7207	4.7233	4.7259	4.7285	4.7311	4.7337	4.7363	4.7389	4.7415	4.7441	3	5	8	10	13
40	4.7467	4.7492	4.7518	4.7544	4.7570	4.7596	4.7622	4.7647	4.7673	4.7699	3	5	8	10	13
41	4.7725	4.7750	4.7776	4.7802	4.7827	4.7853	4.7879	4.7904	4.7930	4.7955	3	5	8	10	13
42	4.7981	4.8007	4.8032	4.8058	4.8083	4.8109	4.8134	4.8160	4.8185	4.8211	3	5	8	10	13
43	4.8236	4.8262	4.8287	4.8313	4.8338	4.8363	4.8389	4.8414	4.8440	4.8465	3	5	8	10	13
44	4.8490	4.8516	4.8541	4.8566	4.8592	4.8617	4.8642	4.8668	4.8693	4.8718	3	5	8	10	13
45	4.8743	4.8769	4.8794	4.8819	4.8844	4.8870	4.8895	4.8920	4.8945	4.8970	3	5	8	10	13
46	4.8996	4.9021	4.9046	4.9071	4.9096	4.9122	4.9147	4.9172	4.9197	4.9222	3	5	8	10	13
47	4.9247	4.9272	4.9298	4.9323	4.9348	4.9373	4.9398	4.9423	4.9448	4.9473	3	5	8	10	13
48	4.9498	4.9524	4.9549	4.9574	4.9599	4.9624	4.9649	4.9674	4.9699	4.9724	3	5	8	10	13
49	4.9749	4.9774	4.9799	4.9825	4.9850	4.9875	4.9900	4.9925	4.9950	4.9975	3	5	8	10	13
50	5.0000	5.0025	5.0050	5.0075	5.0100	5.0125	5.0150	5.0175	5.0201	5.0226	3	5	8	10	13
51	5.0251	5.0276	5.0301	5.0326	5.0351	5.0376	5.0401	5.0426	5.0451	5.0476	3	5	8	10	13
52	5.0502	5.0527	5.0552	5.0577	5.0602	5.0627	5.0652	5.0677	5.0702	5.0728	3	5	8	10	13
53	5.0753	5.0778	5.0803	5.0828	5.0853	5.0878	5.0904	5.0929	5.0954	5.0979	3	5	8	10	13
54	5.1004	5.1030	5.1055	5.1080	5.1105	5.1130	5.1156	5.1181	5.1206	5.1231	3	5	8	10	13
55	5.1257	5.1282	5.1307	5.1332	5.1358	5.1383	5.1408	5.1434	5.1459	5.1484	3	5	8	10	13
56	5.1510	5.1535	5.1560	5.1586	5.1611	5.1637	5.1662	5.1687	5.1713	5.1738	3	5	8	10	13
57	5.1764	5.1789	5.1815	5.1840	5.1866	5.1891	5.1917	5.1942	5.1968	5.1993	3	5	8	10	13
58	5.2019	5.2045	5.2070	5.2096	5.2121	5.2147	5.2173	5.2198	5.2224	5.2250	3	5	8	10	13
59	5.2275	5.2301	5.2327	5.2353	5.2378	5.2404	5.2430	5.2456	5.2482	5.2508	3	5	8	10	13

* Taken from *Statistical Tables for Agricultural, Biological and Medical Research*, 1953, by R.A. FISHER and F. YATES, published by OLIVER and BOYD, Edinburgh. We are indebted to the authors and publishers for permission to reproduce these tables.

% → ↓	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1	2	3	4	5
	Probits														
60	5.2533	5.2559	5.2585	5.2611	5.2637	5.2663	5.2689	5.2715	5.2741	5.2767	3	5	8	10	13
61	5.2793	5.2819	5.2845	5.2871	5.2898	5.2924	5.2950	5.2976	5.3002	5.3029	3	5	8	10	13
62	5.3055	5.3081	5.3107	5.3134	5.3160	5.3186	5.3213	5.3239	5.3266	5.3292	3	5	8	11	13
63	5.3319	5.3345	5.3372	5.3398	5.3425	5.3451	5.3478	5.3505	5.3531	5.3558	3	5	8	11	13
64	5.3585	5.3611	5.3638	5.3665	5.3692	5.3719	5.3745	5.3772	5.3799	5.3826	3	5	8	11	13
65	5.3853	5.3880	5.3907	5.3934	5.3961	5.3989	5.4016	5.4043	5.4070	5.4097	3	5	8	11	14
66	5.4125	5.4152	5.4179	5.4207	5.4234	5.4261	5.4289	5.4316	5.4344	5.4372	3	5	8	11	14
67	5.4399	5.4427	5.4454	5.4482	5.4510	5.4538	5.4565	5.4593	5.4621	5.4649	3	6	8	11	14
68	5.4677	5.4705	5.4733	5.4761	5.4789	5.4817	5.4845	5.4874	5.4902	5.4930	3	6	8	11	14
69	5.4959	5.4987	5.5015	5.5044	5.5072	5.5101	5.5129	5.5158	5.5187	5.5215	3	6	9	11	14
70	5.5244	5.5273	5.5302	5.5330	5.5359	5.5388	5.5417	5.5446	5.5476	5.5505	3	6	9	12	14
71	5.5534	5.5563	5.5592	5.5622	5.5651	5.5681	5.5710	5.5740	5.5769	5.5799	3	6	9	12	15
72	5.5828	5.5858	5.5888	5.5918	5.5948	5.5978	5.6008	5.6038	5.6068	5.6098	3	6	9	12	15
73	5.6128	5.6158	5.6189	5.6219	5.6250	5.6280	5.6311	5.6341	5.6372	5.6403	3	6	9	12	15
74	5.6433	5.6464	5.6495	5.6526	5.6557	5.6588	5.6620	5.6651	5.6682	5.6713	3	6	9	12	16
75	5.6745	5.6776	5.6808	5.6840	5.6871	5.6903	5.6935	5.6967	5.6999	5.7031	3	6	10	13	16
76	5.7063	5.7095	5.7128	5.7160	5.7192	5.7225	5.7257	5.7290	5.7323	5.7356	3	7	10	13	16
77	5.7388	5.7421	5.7454	5.7488	5.7521	5.7554	5.7588	5.7621	5.7655	5.7688	3	7	10	13	17
78	5.7722	5.7756	5.7790	5.7824	5.7858	5.7892	5.7926	5.7961	5.7995	5.8030	3	7	10	14	17
79	5.8064	5.8099	5.8134	5.8169	5.8204	5.8239	5.8274	5.8310	5.8345	5.8381	4	7	11	14	18
80	5.8416	5.8452	5.8488	5.8524	5.8560	5.8596	5.8633	5.8669	5.8705	5.8742	4	7	11	14	18
81	5.8779	5.8816	5.8853	5.8890	5.8927	5.8965	5.9002	5.9040	5.9078	5.9116	4	7	11	15	19
82	5.9154	5.9192	5.9230	5.9269	5.9307	5.9346	5.9385	5.9424	5.9463	5.9502	4	8	12	15	19
83	5.9542	5.9581	5.9621	5.9661	5.9701	5.9741	5.9782	5.9822	5.9863	5.9904	4	8	12	16	20
84	5.9945	5.9986	6.0027	6.0069	6.0110	6.0152	6.0194	6.0237	6.0279	6.0322	4	8	13	17	21
85	6.0364	6.0407	6.0450	6.0494	6.0537	6.0581	6.0625	6.0669	6.0714	6.0758	4	9	13	18	22
86	6.0803	6.0848	6.0893	6.0939	6.0985	6.1031	6.1077	6.1123	6.1170	6.1217	5	9	14	18	23
87	6.1264	6.1311	6.1359	6.1407	6.1455	6.1503	6.1552	6.1601	6.1650	6.1700	5	10	15	19	24
88	6.1750	6.1800	6.1850	6.1901	6.1952	6.2004	6.2055	6.2107	6.2160	6.2212	5	10	15	21	26
89	6.2265	6.2319	6.2372	6.2426	6.2481	6.2536	6.2591	6.2646	6.2702	6.2759	5	11	16	22	27
90	6.2816	6.2873	6.2930	6.2988	6.3047	6.3106	6.3165	6.3225	6.3285	6.3346	6	12	18	24	29
91	6.3408	6.3469	6.3532	6.3595	6.3658	6.3722	6.3787	6.3852	6.3917	6.3984	6	13	19	26	32
92	6.4051	6.4118	6.4187	6.4255	6.4325	6.4395	6.4466	6.4538	6.4611	6.4684	7	14	21	28	35
93	6.4758	6.4833	6.4909	6.4985	6.5063	6.5141	6.5220	6.5301	6.5382	6.5464	8	16	24	31	39
94	6.5548	6.5632	6.5718	6.5805	6.5893	6.5982	6.6072	6.6164	6.6258	6.6352	9	18	27	36	45
95	6.6449	6.6546	6.6646	6.6747	6.6849	6.6954	6.7060	6.7169	6.7279	6.7392					
	97	100	101	102	105	106	109	110	113	115					
96	6.7507	6.7624	6.7744	6.7866	6.7991	6.8119	6.8250	6.8384	6.8522	6.8663					
	117	120	122	125	128	131	134	138	141	145					
97	6.8808	6.8957	6.9110	6.9268	6.9431	6.9600	6.9774	6.9954	7.0141	7.0335					
	149	153	158	163	169	174	180	187	194	202					
98.0	7.0537	7.0558	7.0579	7.0600	7.0621	7.0642	7.0663	7.0684	7.0706	7.0727	2	4	6	8	11
98.1	7.0749	7.0770	7.0792	7.0814	7.0836	7.0858	7.0880	7.0902	7.0924	7.0947	2	4	7	9	11
98.2	7.0969	7.0992	7.1015	7.1038	7.1061	7.1084	7.1107	7.1130	7.1154	7.1177	2	5	7	9	12
98.3	7.1201	7.1224	7.1248	7.1272	7.1297	7.1321	7.1345	7.1370	7.1394	7.1419	2	5	7	10	12
98.4	7.1444	7.1469	7.1494	7.1520	7.1545	7.1571	7.1596	7.1622	7.1648	7.1675	3	5	8	10	13
98.5	7.1701	7.1727	7.1754	7.1781	7.1808	7.1835	7.1862	7.1890	7.1917	7.1945	3	5	8	11	14
98.6	7.1973	7.2001	7.2029	7.2058	7.2086	7.2115	7.2144	7.2173	7.2203	7.2232	3	6	9	12	14
98.7	7.2262	7.2292	7.2322	7.2353	7.2383	7.2414	7.2445	7.2476	7.2508	7.2539	3	6	9	12	15
98.8	7.2571	7.2603	7.2636	7.2668	7.2701	7.2734	7.2768	7.2801	7.2835	7.2869	3	7	10	13	17
98.9	7.2904	7.2938	7.2973	7.3009	7.3044	7.3080	7.3116	7.3152	7.3189	7.3226	4	7	11	14	18
99.0	7.3263	7.3301	7.3339	7.3378	7.3416	7.3455	7.3495	7.3535	7.3575	7.3615	4	8	12	16	20
99.1	7.3656	7.3698	7.3739	7.3781	7.3824	7.3867	7.3911	7.3954	7.3999	7.4044	4	9	13	17	22
99.2	7.4089	7.4135	7.4181	7.4228	7.4276	7.4324	7.4372	7.4422	7.4471	7.4522	5	10	14	19	24
99.3	7.4573	7.4624	7.4677	7.4730	7.4783	7.4838	7.4893	7.4949	7.5006	7.5063	5	11	16	22	27
99.4	7.5121	7.5181	7.5241	7.5302	7.5364	7.5427	7.5491	7.5556	7.5622	7.5690	6	13	19	25	32
99.5	7.5758	7.5828	7.5899	7.5972	7.6045	7.6121	7.6197	7.6276	7.6356	7.6437					
99.6	7.6521	7.6606	7.6693	7.6783	7.6874	7.6968	7.7065	7.7164	7.7266	7.7370					
99.7	7.7478	7.7589	7.7703	7.7822	7.7944	7.8070	7.8202	7.8338	7.8480	7.8627					
99.8	7.8782	7.8943	7.9112	7.9290	7.9478	7.9677	7.9889	8.0115	8.0357	8.0618					
99.9	8.0902	8.1214	8.1559	8.1947	8.2389	8.2905	8.3528	8.4316	8.5401	8.7190					

The Normal Distribution — Probit Transformation
Weighting coefficients and probit values to be used for final adjustments*

Expected probit Y	Minimum working probit $Y-P/Z$	Range $1/Z$	Maximum working probit $Y+Q/Z$	Weighting coefficient Z^2/PQ	Expected probit Y	Minimum working probit $Y-P/Z$	Range $1/Z$	Maximum working probit $Y+Q/Z$	Weighting coefficient Z^2/PQ
1.1	0.8579	5034	5035	0.00082	5.0	3.7467	2.5066	6.2533	0.63662
1.2	0.9522	3425	3426	.00118	5.1	3.7401	2.5192	6.2593	.63431
1.3	1.0462	2354	2355	.00167	5.2	3.7186	2.5573	6.2759	.62742
1.4	1.1400	1634	1635	.00235	5.3	3.6798	2.6220	6.3018	.61609
1.5	1.2335	1146	1147	.00327	5.4	3.6203	2.7154	6.3357	.60052
1.6	1.3266	811.5	812.8	0.00451	5.5	3.5360	2.8404	6.3764	0.58099
1.7	1.4194	580.5	581.9	.00614	5.6	3.4220	3.0010	6.4230	.55788
1.8	1.5118	419.4	420.9	.00828	5.7	3.2724	3.2025	6.4749	.53159
1.9	1.6038	306.1	307.7	.01104	5.8	3.0794	3.4519	6.5313	.50260
2.0	1.6954	225.6	227.3	.01457	5.9	2.8335	3.7582	6.5917	.47144
2.1	1.7866	168.00	169.79	0.01903	6.0	2.5230	4.1327	6.6557	0.43863
2.2	1.8772	126.34	128.22	.02459	6.1	2.1324	4.5903	6.7227	.40474
2.3	1.9673	95.96	97.93	.03143	6.2	1.6429	5.1497	6.7926	.37031
2.4	2.0568	73.62	75.68	.03977	6.3	1.0295	5.8354	6.8649	.33589
2.5	2.1457	57.05	59.20	.04979	6.4	0.2606	6.6788	6.9394	.30199
2.6	2.2340	44.654	46.888	0.06169	6.5	—0.705	7.721	7.0158	0.26907
2.7	2.3214	35.302	37.623	.07563	6.6	—1.921	9.015	7.0940	.23753
2.8	2.4081	28.189	30.597	.09179	6.7	—3.459	10.633	7.1739	.20774
2.9	2.4938	22.736	25.230	.11026	6.8	—5.411	12.666	7.2551	.17994
3.0	2.5786	18.522	21.101	.13112	6.9	—7.902	15.240	7.3376	.15436
3.1	2.6624	15.240	17.902	0.15436	7.0	—11.101	18.522	7.4214	0.13112
3.2	2.7449	12.666	15.411	.17994	7.1	—15.230	22.736	7.5062	.11026
3.3	2.8261	10.633	13.459	.20774	7.2	—20.597	28.189	7.5919	.09179
3.4	2.9060	9.015	11.921	.23753	7.3	—27.623	35.302	7.6786	.07564
3.5	2.9842	7.721	10.705	.26907	7.4	—36.888	44.654	7.7661	.06168
3.6	3.0606	6.6788	9.7394	0.30199	7.5	—49.20	57.05	7.8543	0.04979
3.7	3.1351	5.8354	8.9705	.33589	7.6	—65.68	73.62	7.9432	.03977
3.8	3.2074	5.1497	8.3571	.37031	7.7	—87.93	95.96	8.0327	.03143
3.9	3.2773	4.5903	7.8676	.40474	7.8	—118.22	126.34	8.1228	.02458
4.0	3.3443	4.1327	7.4770	.43863	7.9	—159.79	168.00	8.2134	.01903
4.1	3.4083	3.7582	7.1665	0.47144	8.0	—217.3	225.6	8.3046	0.01457
4.2	3.4687	3.4519	6.9206	.50260	8.1	—297.7	306.1	8.3962	.01104
4.3	3.5251	3.2025	6.7276	.53159	8.2	—410.9	419.4	8.4882	.00828
4.4	3.5770	3.0010	6.5780	.55788	8.3	—571.9	580.5	8.5806	.00614
4.5	3.6236	2.8404	6.4640	.58099	8.4	—802.8	811.5	8.6734	.00451
4.6	3.6643	2.7154	6.3797	0.60052	8.5	—1137	1146	8.7666	0.00327
4.7	3.6982	2.6220	6.3202	.61609	8.6	—1625	1634	8.8600	.00235
4.8	3.7241	2.5573	6.2814	.62741	8.7	—2345	2354	8.9538	.00167
4.9	3.7407	2.5192	6.2599	.63431	8.8	—3416	3425	9.0478	.00118
5.0	3.7467	2.5066	6.2533	.63662	8.9	—5025	5034	9.1421	.00082

* Taken from *Statistical Tables for Agricultural, Biological and Medical Research*, 1953, by R.A. FISHER and F. YATES, published by OLIVER and BOYD, Edinburgh. We are indebted to the authors and publishers for permission to reproduce these tables.

Normal probability integral = 1/2 P*

1/2 P = Area under the normal distribution between the ordinates c = ∞ and c, or c = -∞ and -c

c → ↓		0	1	2	3	4	5	6	7	8	9
		1/2 P									
0.0	0.	50000	49601	49202	48803	48405	48006	47608	47210	46812	46414
0.1		46017	45620	45224	44828	44433	44038	43644	43251	42858	42465
0.2		42074	41683	41294	40905	40517	40129	39743	39358	38974	38591
0.3		38209	37828	37448	37070	36693	36317	35942	35569	35197	34827
0.4		34458	34090	33724	33360	32997	32636	32276	31918	31561	31207
0.5		30854	30503	30153	29806	29460	29116	28774	28434	28096	27760
0.6		27425	27093	26763	26435	26109	25785	25463	25143	24825	24510
0.7		24196	23885	23576	23270	22965	22663	22363	22065	21770	21476
0.8		21186	20897	20611	20327	20045	19766	19489	19215	18943	18673
0.9		18406	18141	17879	17619	17361	17106	16853	16602	16354	16109
1.0		15866	15625	15386	15151	14917	14686	14457	14231	14007	13786
1.1		13567	13350	13136	12924	12714	12507	12302	12100	11900	11702
1.2		11507	11314	11123	10935	10749	10565	10383	10204	10027	98525
1.3	0.0	96800	95098	93418	91759	90123	88508	86915	85343	83793	82264
1.4		80757	79270	77804	76359	74934	73529	72145	70781	69437	68112
1.5		66807	65522	64255	63008	61780	60571	59380	58208	57053	55917
1.6		54799	53699	52616	51551	50503	49471	48457	47460	46479	45514
1.7		44565	43633	42716	41815	40930	40059	39204	38364	37538	36727
1.8		35930	35148	34380	33625	32884	32157	31443	30742	30054	29379
1.9		28717	28067	27429	26803	26190	25588	24998	24419	23852	23295
2.0		22750	22216	21692	21178	20675	20182	19699	19226	18763	18309
2.1		17864	17429	17003	16586	16177	15778	15386	15003	14629	14262
2.2		13903	13553	13209	12874	12545	12224	11911	11604	11304	11011
2.3		10724	10444	10170	99031	96419	93867	91375	88940	86563	84242
2.4	0.0²	81975	79763	77603	75494	73436	71428	69469	67557	65691	63872
2.5		62097	60366	58677	57031	55426	53861	52336	50849	49400	47988
2.6		46612	45271	43965	42692	41453	40246	39070	37926	36811	35726
2.7		34670	33642	32641	31667	30720	29798	28901	28028	27179	26354
2.8		25551	24771	24012	23274	22557	21860	21182	20524	19884	19262
2.9		18658	18071	17502	16948	16411	15889	15382	14890	14412	13949
3.0		13499	13062	12639	12228	11829	11442	11067	10703	10350	10008
3.1	0.0³	96760	93544	90426	87403	84474	81635	78885	76219	73638	71136
3.2		68714	66367	64095	61895	59765	57703	55706	53774	51904	50094
3.3		48342	46648	45009	43423	41889	40406	38971	37584	36243	34946
3.4		33693	32481	31311	30179	29086	28029	27009	26023	25071	24151
3.5		23263	22405	21577	20778	20006	19262	18543	17849	17180	16534
3.6		15911	15310	14730	14171	13632	13112	12611	12128	11662	11213
3.7		10780	10363	99611	95740	92010	88417	84957	81624	78414	75324
3.8	0.0⁴	72348	69483	66726	64072	61517	59059	56694	54418	52228	50122
3.9		48096	46148	44274	42473	40741	39076	37475	35936	34458	33037
4.0		31671	30359	29099	27888	26726	25609	24536	23507	22518	21569
4.1		20658	19783	18944	18138	17365	16624	15912	15230	14575	13948
4.2		13346	12769	12215	11685	11176	10689	10221	97736	93447	89337
4.3	0.0⁵	85399	81627	78015	74555	71241	68069	65031	62123	59340	56675
4.4		54125	51685	49350	47117	44979	42935	40980	39110	37322	35612
4.5		33977	32414	30920	29492	28127	26823	25577	24386	23249	22162
4.6		21125	20133	19187	18283	17420	16597	15810	15060	14344	13660
4.7		13008	12386	11792	11226	10686	10171	96796	92113	87648	83391
4.8	0.0⁶	79333	75465	71779	68267	64920	61731	58693	55799	53043	50418
4.9		47918	45538	43272	41115	39061	37107	35247	33476	31792	30190

Probability P

P = Area under the normal distribution outside the ordinates -c and c

P → ↓		0.00	0.01	0.02	0.03	0.04	0.05	0.06	0.07	0.08	0.09
		Deviation c									
0.0	∞	2.575829	2.326348	2.170090	2.053749	1.959964	1.880794	1.811911	1.750686	1.695398	
0.1	1.644854	1.598193	1.554774	1.514102	1.475791	1.439531	1.405072	1.372204	1.340755	1.310579	
0.2	1.281552	1.253565	1.226528	1.200359	1.174987	1.150349	1.126391	1.103063	1.080319	1.058122	
0.3	1.036433	1.015222	0.994458	0.974114	0.954165	0.934589	0.915365	0.896473	0.877896	0.859617	
0.4	0.841621	0.823894	0.806421	0.789192	0.772193	0.755415	0.738847	0.722479	0.706303	0.690309	
0.5	0.674490	0.658838	0.643345	0.628006	0.612813	0.597760	0.582842	0.568051	0.553385	0.538836	
0.6	0.524401	0.510073	0.495850	0.481727	0.467699	0.453762	0.439913	0.426148	0.412463	0.398855	
0.7	0.385320	0.371856	0.358459	0.345126	0.331853	0.318639	0.305481	0.292375	0.279319	0.266311	
0.8	0.253347	0.240426	0.227545	0.214702	0.201893	0.189118	0.176374	0.163658	0.150969	0.138304	
0.9	0.125661	0.113039	0.100434	0.087845	0.075270	0.062707	0.050154	0.037608	0.025069	0.012533	

Very small values of P

P	.	.	0.001	0.000 1	0.000 01	0.000 001	0.000 000 1	0.000 000 01	0.000 000 001
c	.	.	3.29053	3.89059	4.41717	4.89164	5.32672	5.73073	6.10941

* Taken from Statistical Tables for Agricultural, Biological and Medical Research, 1953, by R.A. FISHER and F. YATES, published by OLIVER and BOYD, Edinburgh. We are indebted to the authors and publishers for permission to reproduce these tables.

The values of *P* given below correspond to the probabilities *P* of the normal distribution

1. Distribution of *t**

Degree of freedom <i>n</i>	Probability <i>P</i>												
	0.90	0.80	0.70	0.60	0.50	0.40	0.30	0.20	0.10	0.05	0.02	0.01	0.001
	Deviation <i>t</i>												
1	0.158	0.325	0.510	0.727	1.000	1.376	1.963	3.078	6.314	12.706	31.821	63.657	636.619
2	0.142	0.289	0.445	0.617	0.816	1.061	1.386	1.886	2.920	4.303	6.965	9.925	31.598
3	0.137	0.277	0.424	0.584	0.765	0.978	1.250	1.638	2.353	3.182	4.541	5.841	12.924
4	0.134	0.271	0.414	0.569	0.741	0.941	1.190	1.533	2.132	2.776	3.747	4.604	8.610
5	0.132	0.267	0.408	0.559	0.727	0.920	1.156	1.476	2.015	2.571	3.365	4.032	6.869
6	0.131	0.265	0.404	0.553	0.718	0.906	1.134	1.440	1.943	2.447	3.143	3.707	5.959
7	0.130	0.263	0.402	0.549	0.711	0.896	1.119	1.415	1.895	2.365	2.998	3.499	5.408
8	0.130	0.262	0.399	0.546	0.706	0.889	1.108	1.397	1.860	2.306	2.896	3.355	5.041
9	0.129	0.261	0.398	0.543	0.703	0.883	1.100	1.383	1.833	2.262	2.821	3.250	4.781
10	0.129	0.260	0.397	0.542	0.700	0.879	1.093	1.372	1.812	2.228	2.764	3.169	4.587
11	0.129	0.260	0.396	0.540	0.697	0.876	1.088	1.363	1.796	2.201	2.718	3.106	4.437
12	0.128	0.259	0.395	0.539	0.695	0.873	1.083	1.356	1.782	2.179	2.681	3.055	4.318
13	0.128	0.259	0.394	0.538	0.694	0.870	1.079	1.350	1.771	2.160	2.650	3.012	4.221
14	0.128	0.258	0.393	0.537	0.692	0.868	1.076	1.345	1.761	2.145	2.624	2.977	4.140
15	0.128	0.258	0.393	0.536	0.691	0.866	1.074	1.341	1.753	2.131	2.602	2.947	4.073
16	0.128	0.258	0.392	0.535	0.690	0.865	1.071	1.337	1.746	2.120	2.583	2.921	4.015
17	0.128	0.257	0.392	0.534	0.689	0.863	1.069	1.333	1.740	2.110	2.567	2.898	3.965
18	0.127	0.257	0.392	0.534	0.688	0.862	1.067	1.330	1.734	2.101	2.552	2.878	3.922
19	0.127	0.257	0.391	0.533	0.688	0.861	1.066	1.328	1.729	2.093	2.539	2.861	3.883
20	0.127	0.257	0.391	0.533	0.687	0.860	1.064	1.325	1.725	2.086	2.528	2.845	3.850
21	0.127	0.257	0.391	0.532	0.686	0.859	1.063	1.323	1.721	2.080	2.518	2.831	3.819
22	0.127	0.256	0.390	0.532	0.686	0.858	1.061	1.321	1.717	2.074	2.508	2.819	3.792
23	0.127	0.256	0.390	0.532	0.685	0.858	1.060	1.319	1.714	2.069	2.500	2.807	3.767
24	0.127	0.256	0.390	0.531	0.685	0.857	1.059	1.318	1.711	2.064	2.492	2.797	3.745
25	0.127	0.256	0.390	0.531	0.684	0.856	1.058	1.316	1.708	2.060	2.485	2.787	3.725
26	0.127	0.256	0.390	0.531	0.684	0.856	1.058	1.315	1.706	2.056	2.479	2.779	3.707
27	0.127	0.256	0.389	0.531	0.684	0.855	1.057	1.314	1.703	2.052	2.473	2.771	3.690
28	0.127	0.256	0.389	0.530	0.683	0.855	1.056	1.313	1.701	2.048	2.467	2.763	3.674
29	0.127	0.256	0.389	0.530	0.683	0.854	1.055	1.311	1.699	2.045	2.462	2.756	3.659
30	0.127	0.256	0.389	0.530	0.683	0.854	1.055	1.310	1.697	2.042	2.457	2.750	3.646
40	0.126	0.255	0.388	0.529	0.681	0.851	1.050	1.303	1.684	2.021	2.423	2.704	3.551
60	0.126	0.254	0.387	0.527	0.679	0.848	1.046	1.296	1.671	2.000	2.390	2.660	3.460
120	0.126	0.254	0.386	0.526	0.677	0.845	1.041	1.289	1.658	1.980	2.358	2.617	3.373
∞	0.126	0.253	0.385	0.524	0.674	0.842	1.036	1.282	1.645	1.960	2.326	2.576	3.291

2. Distribution of χ^2 *

Degree of freedom <i>n</i>	Probability <i>P</i>													
	0.99	0.98	0.95	0.90	0.80	0.70	0.50	0.30	0.20	0.10	0.05	0.02	0.01	0.001
	χ^2													
1	0.0*157	0.0*628	0.00393	0.0158	0.0642	0.148	0.455	1.074	1.642	2.706	3.841	5.412	6.635	10.827
2	0.0201	0.0404	0.103	0.211	0.446	0.713	1.386	2.408	3.219	4.605	5.991	7.824	9.210	13.815
3	0.115	0.185	0.352	0.584	1.005	1.424	2.366	3.665	4.642	6.251	7.815	9.837	11.345	16.266
4	0.297	0.429	0.711	1.064	1.649	2.195	3.357	4.878	5.989	7.779	9.488	11.668	13.277	18.467
5	0.554	0.752	1.145	1.610	2.343	3.000	4.351	6.064	7.289	9.236	11.070	13.388	15.086	20.515
6	0.872	1.134	1.635	2.204	3.070	3.828	5.348	7.231	8.558	10.645	12.592	15.033	16.812	22.457
7	1.239	1.564	2.167	2.833	3.822	4.671	6.346	8.383	9.803	12.017	14.067	16.622	18.475	24.322
8	1.646	2.032	2.733	3.490	4.594	5.527	7.344	9.524	11.030	13.362	15.507	18.168	20.090	26.125
9	2.088	2.532	3.325	4.168	5.380	6.393	8.343	10.656	12.242	14.684	16.919	19.679	21.666	27.877
10	2.558	3.059	3.940	4.865	6.179	7.267	9.342	11.781	13.442	15.987	18.307	21.161	23.209	29.588
11	3.053	3.609	4.575	5.578	6.989	8.148	10.341	12.899	14.631	17.275	19.675	22.618	24.725	31.264
12	3.571	4.178	5.226	6.304	7.807	9.034	11.340	14.011	15.812	18.549	21.026	24.054	26.217	32.909
13	4.107	4.765	5.892	7.042	8.634	9.926	12.340	15.119	16.985	19.812	22.362	25.472	27.688	34.528
14	4.660	5.368	6.571	7.790	9.467	10.821	13.339	16.222	18.151	21.064	23.685	26.873	29.141	36.123
15	5.229	5.985	7.261	8.547	10.307	11.721	14.339	17.322	19.311	22.307	24.996	28.259	30.578	37.697
16	5.812	6.614	7.962	9.312	11.152	12.624	15.338	18.418	20.465	23.542	26.296	29.633	32.000	39.252
17	6.408	7.255	8.672	10.085	12.002	13.531	16.338	19.511	21.615	24.769	27.587	30.995	33.409	40.790
18	7.015	7.906	9.390	10.865	12.857	14.440	17.338	20.601	22.760	25.989	28.869	32.346	34.805	42.312
19	7.633	8.567	10.117	11.651	13.716	15.352	18.338	21.689	23.900	27.204	30.144	33.687	36.191	43.820
20	8.260	9.237	10.851	12.443	14.578	16.266	19.337	22.775	25.038	28.412	31.410	35.020	37.566	45.315
21	8.897	9.915	11.591	13.240	15.445	17.182	20.337	23.858	26.171	29.615	32.671	36.343	38.932	46.797
22	9.542	10.600	12.338	14.041	16.314	18.101	21.337	24.939	27.301	30.813	33.924	37.659	40.289	48.268
23	10.196	11.293	13.091	14.848	17.187	19.021	22.337	26.018	28.429	32.007	35.172	38.968	41.638	49.728
24	10.856	11.992	13.848	15.659	18.062	19.943	23.337	27.096	29.553	33.196	36.415	40.270	42.980	51.179
25	11.524	12.697	14.611	16.473	18.940	20.867	24.337	28.172	30.675	34.382	37.652	41.566	44.314	52.620
26	12.198	13.409	15.379	17.292	19.820	21.792	25.336	29.246	31.795	35.563	38.885	42.856	45.642	54.052
27	12.879	14.125	16.151	18.114	20.703	22.719	26.336	30.319	32.912	36.741	40.113	44.140	46.963	55.476
28	13.565	14.847	16.928	18.939	21.588	23.647	27.336	31.391	34.027	37.916	41.337	45.419	48.278	56.893
29	14.256	15.574	17.708	19.768	22.475	24.577	28.336	32.461	35.139	39.087	42.557	46.693	49.588	58.302
30	14.953	16.306	18.493	20.599	23.364	25.508	29.336	33.530	36.250	40.256	43.773	47.962	50.892	59.703

* Taken from *Statistical Tables for Agricultural, Biological and Medical Research*, 1953, by R. A. FISHER and F. YATES, published by OLIVER and BOYD, Edinburgh. We are indebted to the authors and publishers for permission to reproduce these tables.

General

The calculation of probabilities by statistical methods is essential to the proper interpretation of observational data which, although following certain basic laws, are nevertheless subject to modification by unknown factors, or "chance". This is true not only for the empirical sciences, both the exact and the biological, but also in a wider sense for the abstract sciences:

On peut même dire, à parler en rigueur, que presque toutes nos connaissances ne sont que probables; et dans le petit nombre des choses que nous pouvons savoir avec certitude, dans les sciences mathématiques elles-mêmes, les principaux moyens de parvenir à la vérité, l'induction et l'analogie, se fondent sur les probabilités... (LAPLACE, 1820)¹.

The distrust with which the doctor often views statistics probably has its origin partly in the well-known saying that "statistics can prove anything". On the other hand a certain dislike of statistics is no doubt a result of the general preference of doctors for intuitive reasoning. This feeling has no logical basis. The science of statistics constitutes one of the most useful branches of mathematics; its basic techniques for the disciplined orientation of observational data can readily be mastered. It should not be overlooked that every diagnosis is the result of a conscious or unconscious assessment of probabilities.

The deprecatory saying quoted above without doubt has its origin in mistaken applications of statistical methods, and in erroneous or unjustified interpretations of statistical treatments. The statistical method is simply another scientific method and as such cannot prove or disprove anything. On the other hand it is the sole method whereby magnitudes subject to chance variation (stochastic magnitudes) may be judged according to hard and fast rules based on logical mathematical considerations. Much nearer the truth therefore is the view that only with a knowledge of statistics may one presume that an investigation has proved anything. One should never overlook the extent to which subconscious wishes and deeply-rooted prejudices, even in the most cautious and sceptical of observers, can cause certain chances to be rated too highly. The most careful of investigators can be misled by such psychological vectors, and only by the exercise of considerable self-control can they be avoided:

Le sentiment par lequel l'homme s'est placé longtemps au centre de l'univers, en se considérant comme l'objet spécial des soins de la nature, porte chaque individu à se faire le centre d'une sphère plus ou moins étendue, et à croire que le hasard a pour lui des préférences. Soutenus par cette opinion, les joueurs exposent souvent des sommes considérables à des jeux dont ils savent que les chances leur sont contraires. Dans la conduite de la vie, une semblable opinion peut quelquefois avoir des avantages; mais le plus souvent elle conduit à des entreprises funestes. Ici, comme en tout, les illusions sont dangereuses et la vérité seule est généralement utile.

Un des grands avantages du Calcul des Probabilités est d'apprendre à se défier des premiers aperçus. Comme on reconnaît qu'ils trompent souvent lorsqu'on peut les soumettre au calcul, on doit en conclure que sur d'autres objets il ne faut s'y livrer qu'avec une circonspection extrême. (LAPLACE, 1820)¹.

The "wish as father to the thought", disguised as "our experience", "our view", "our conviction", etc. and supported by numerous percentages, has thus much to be blamed for, even though it may constitute an indispensable spur to further research. One need only reflect on the wealth of improved treatments, new drugs, etc. announced in the medical press and greeted with such enthusiasm, only to be subsequently abandoned and forgotten. A crass example of recent times is furnished by retrolental fibroplasia². Unknown before 1936, it is today recognized as one of the most frequent causes of infantile blindness. The effect of light, deficiency of vitamin A, deficiency of vitamin E and water-soluble vitamins, cow's milk, too little and too much oxygen, have all been put forward as possible causes of this condition. The methods of treatment have varied accordingly, and have included the un-

fortunate experiment with ACTH and cortisone. An adequate attempt to evaluate any of these methods of treatment by statistical comparison with untreated controls has yet to be made, for the simple reason that none of the investigators would allow what he considered to be the sole correct treatment to be withheld from any of the threatened children. The paradoxical situation finally emerged that neither of the two clinical groups with diametrically opposed views – the one viewing oxygen deficiency as the aetiological factor, the other oxygen excess – could bring itself, on these ethical grounds, to agree to tests involving untreated controls³.

Principles of statistics

The fundamental conception of statistics is that of an infinitely large series of measurements, or *population*. Since all observational data is subject to influence by uncontrollable and variable chance factors, the values recorded in a series of measurements exhibit corresponding variations. If the mean value is calculated the individual values will be seen to be more or less closely distributed around it. Since the chance factors operate equally in a positive or negative fashion, the distribution is symmetrical. The larger the number of measurements the closer will the mean value approach the "true" value of the measured object. Only with an infinite number of measurements however will it be identical with the "true" value.

In practice, instead of the axiomatic requirement of an infinite series of measurements, a limited number of tests, known as *random samples*, must suffice. The investigator will at once enquire what relation the sample bears to the whole population, i.e. how representative it is of the population. The comparison between these two, random sample and population, is the basic principle of statistics. In this respect statistics differs from the pure calculation of probabilities, which is concerned only with theoretical populations and their distributions.

The above-mentioned distribution of experimental errors takes the form of a bell-shaped curve and is known as the normal distribution. Many other kinds of distributions are known but only few of them have any considerable practical application. These are the BERNOULLI or binomial distribution, the POISSON distribution, the *t*-distribution, the χ^2 -distribution, and the γ - or closely related *F*-distribution. These distributions can only be described in detail with the aid of higher mathematics. The reader should not allow himself to be deterred however, since of the practical methods derived from them, a large number may be learnt intuitively and without any great knowledge of mathematics.

The various theoretical distributions are characterized quite sharply by certain constants, known as parameters. The normal distribution, for example, is defined unequivocally by its parameters mean value and variance; any desired individual value may thereby be calculated. To turn now to the population against which the sample must be compared, the form of this may be constructed from one of the theoretical distributions, provided that the probabilities influencing the sample can be deduced from the hypothesis which is to be put to the test. In genetics, for example, this is the normal procedure, but not as a rule in other branches of science where only the results from a limited number of experimental series are available. In these circumstances either the sample is compared with an arbitrarily chosen test distribution, or the latter is dispensed with and a population built up from a number of different experimental series.

One of the problems most frequently encountered in medicine consists in the comparison of two or more experimental series with the object of establishing whether a concrete difference, or variation, exists between them, such as in the testing of drugs or methods of treatment. There are several ways in which the

¹ LAPLACE, *Théorie analytique des probabilités*, Paris, 1820. ² CLIFFORD, S. H., *J. Pediat.*, **43**, 237, 1953. ³ Retrolental fibroplasia in premature infants has since been the subject of a statistical survey in Great Britain, in conjunction with animal experiments designed to test the most likely hypothesis, viz. asphyxia of the retinal tissues due to the custom of rearing such infants in an atmosphere rich in oxygen. The results have confirmed that this is indeed the cause, and the disease has virtually disappeared since the concentration of oxygen to which the children are exposed has been reduced to 40% or less. Cf. *Report of the Medical Research Council 1953-1954*, London, 1955, page 15.

significance of variations may be put to the test. One of the best is the use of the so-called null-hypothesis, examples of which will be discussed later. This method poses the question: what is the probability that an observed value (e.g. a mean or the difference between two means) is solely due to chance or, in other words, is not (null) due to "non-chance"? If this probability is very small, then the non-fortuitous nature of the series being tested has been proved. It falls to the investigator to decide on the limiting probabilities, although there is now general agreement on the use of 5% or 1% as the limiting values for significance. In medicine 5% can be considered as sufficient.

Statistical evaluation cannot produce more information from observational data than the data already contain. It can, however, lead to the discovery, in a mass of observational data, of inter-relations or regularities which would otherwise remain hidden. Here, however, it must not be forgotten that the process is basically that of mathematical factors suggesting the existence of certain underlying causes, or of allowing such causes to be presumed. The causes themselves can never be demonstrated statistically. Mathematical analogy is not causality.

The statistical treatment of the observational data must conform to the logical structure of the investigation. Conversely, the planning and execution of the experiments should be appropriate to the subsequent statistical evaluation. The close interdependence between these two aspects is unfortunately much too little appreciated by many workers. It is just as important that this factor should be borne in mind in planning an investigation as it is to bear in mind the type of clinical, chemical or physical method which it is proposed to use. The result can only be an improvement in experimental efficiency and a reduction in experimental outlay. Long and painstaking experimentation has often failed to yield a decisive answer to a problem through the simple neglect of this consideration.

Nomenclature

Before passing to more concrete matters a word must be said on the subject of nomenclature. The unabbreviated terms for statistical conceptions are the same in almost all languages. Although differences may occur here and there, the meaning is always clear and confusion is unlikely to arise. Where symbols are concerned, however, a great deal of confusion reigns. There are differences from country to country and even from author to author. The choice of symbols used in these *Tables* represents a compromise in which the guiding principle has been to make the study as easy as possible for the beginner.

In order to emphasize the distinction between random samples and expected distributions, all symbols and names associated with the former are printed in grotesque type and those associated with the latter in *italics*. Greek letters have also been used occasionally for the symbols connected with distributions. The quantities associated with random samples are known as statistical parameters (statistics).

Mean and Variance

The most important of the parameters for collectives (populations) used in statistics are the **arithmetical mean**, also called simply the mean, and the mean quadratic deviation, known as the **standard deviation**, or its square, the mean quadratic variation, known as the **variance**.

Symbols:	Sample	Trial distribution
Arithmetical mean	\bar{x}	m
Standard deviation	s	σ
Variance	s^2	σ^2

The mean \bar{x} of a sample with individual values x_1, x_2, x_3, \dots is defined as the quotient: sum of all individual values divided by their total number N , or

$$\bar{x} = \frac{1}{N} S(x) \tag{1}$$

(S = summation sign: $S(x) = x_1 + x_2 + x_3 + \dots$)

The variance s^2 of a sample is defined as the quotient: sum of the squares of the deviations of the individual values from the mean, divided by the total number of individual values less 1. The standard deviation s is the square root of the variance s^2 .

$$s^2 = \frac{1}{N-1} S(x - \bar{x})^2 \tag{2a}$$

It is more convenient to calculate the variance from the following formula than from (2a):

$$s^2 = \frac{1}{N-1} \left(S(x^2) - \bar{x} S(x) \right) \tag{2b}$$

or

$$s^2 = \frac{1}{N-1} \left(S(x^2) - \frac{[S(x)]^2}{N} \right) \tag{2c}$$

For large samples and samples divided into classes other convenient formulae may be found in the literature*.

The mean is an abstract conception which by itself has little meaning in the biological sciences. What is the significance, for example, of a mean height of 53 inches (the normal) when all 9-year old boys measured are either taller or shorter than this? In biological populations, where a certain variation is to be expected, an average normal range embracing the majority of normal variations is clearly of more significance. The measure for the delimitation of this normal range is the standard deviation (σ or s). The mean is thus only of statistical significance in combination with the standard deviation.

The delimitation of the normal range follows from the theory of the normal distribution (q.v.) but the fixing of the actual limiting values is a matter for agreement. In a normally distributed population 95.5% of all normal (chance) variations are expected to fall within the range: mean $\pm 2\sigma$. The probability that a value lying outside these limits represents a normal deviation which has "slipped" in by chance is thus $100 - 95.5 = 4.5\%$. In 100 measurements only 4.5 such extreme deviations may therefore be expected. If 20 values, for example, lie outside the 5% limit it can be assumed that some factor other than pure chance is involved. The testing of such variations will be demonstrated later.

In biology the limit already mentioned, 4.5% or mean $\pm 2\sigma$, should suffice. It is not usual to start with integral standard deviations since this produces percentage limits which are fractional. It is therefore now usual to adopt the limits of 5% or 1%, of which the former can without hesitation be equated to 2σ . The corresponding deviations from the mean are 1.96 and 2.57 times the standard deviation. The table of probabilities P on page 29 allows the probabilities corresponding to any particular deviation to be found, and vice versa. The limits given are those in general use, but the investigator is free to choose others, although for the sake of comparability it is preferable to keep to the usual values.

If the limits are drawn symmetrically above and below the mean it is obvious that the mean should represent not only the numerical average of the individual values but should also stand approximately in the middle of these values. Only in these circumstances is such a symmetrical delimitation logically justified (fig. 1).

Fig. 1



If this is not the case, then the position of the limits appears at least suspicious and may even be quite irrational, as example 1 (fig. 2) shows. In this case a single extraneous value has displaced the mean in the "wrong" direction and affected the standard deviation so markedly that one of the limits (mean $\pm 2s$) even falls below zero.

* See also Appendix, page 47.

Example 1. Series of individual experimental values (centimetres). For demonstration purposes the mean and variance have been calculated from the formulae **1** and **2a, b, c**. $N = 10$; $N - 1 = 9$.

Individual values	Deviation of the individual values from the mean	Squares of the deviations	Squares of the individual values
x	$(x - \bar{x})$	$(x - \bar{x})^2$	x^2
1.2	- 1.02	1.0404	1.44
1.1	- 1.12	1.2544	1.21
1.3	- 0.92	0.8464	1.69
2.4	+ 0.18	0.0324	5.76
2.1	- 0.12	0.0144	4.41
1.8	- 0.42	0.1764	3.24
3	+ 0.78	0.6084	9
2	- 0.22	0.0484	4
6	+ 3.78	14.2884	36
1.3	- 0.92	0.8464	1.69
22.2 = $S(x)$	0.00 = $S(x - \bar{x})$	19.1560 = $S(x - \bar{x})^2$	68.44 = $S(x^2)$

Mean $\bar{x} = S(x) \div 10 = 2.22$

Variance s^2 according to formula **2a** = $S(x - \bar{x})^2 \div 9 = 2.13$

Variance s^2 according to formula **2b** = $(S(x^2) - \bar{x} S(x)) \div 9 = (68.44 - 2.22 \times 22.2) \div 9 = (68.44 - 49.284) \div 9 = 19.1560 : 9 = 2.13$

Variance s^2 according to formula **2c** = $(S(x^2) - \frac{[S(x)]^2}{N}) \div 9 = (68.44 - \frac{492.84}{10}) \div 9 = (68.44 - 49.284) \div 9 = 19.1560 : 9 = 2.13$

Standard deviation = $\sqrt{s^2} = 1.46$

“Normal” range $\bar{x} \pm 2s = -0.7$ to $+ 5.14$

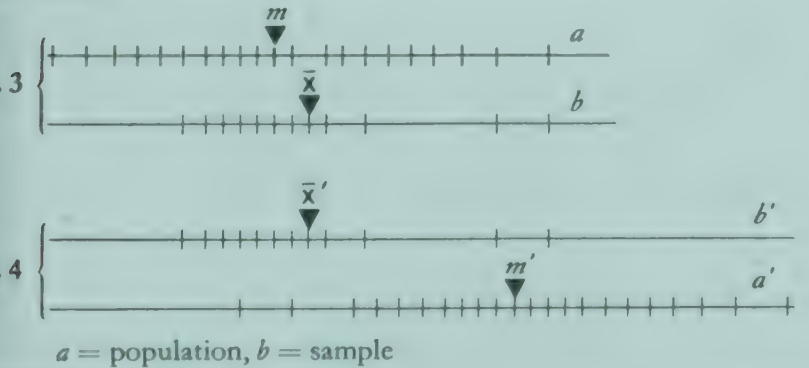
for check of the calculation from formula **2a** (sum must be equal to zero).

It is at once obvious from this example that the calculation of the variance from the formulae **2b** or **2c** is much simpler since x^2 as a rule has fewer decimal places than $(x - \bar{x})^2$ and the repeated subtraction to obtain $(x - \bar{x})$ is avoided.



Even though it may appear somewhat elementary it is advisable to make a quick check of the sample mean with respect to its symmetrical position among the individual values. This can be done graphically, or mathematically by means of $(x - \bar{x})$. In the latter case it is only necessary to make a rough calculation of the differences. If the plus and minus totals are about equal it may be assumed that the mean does actually lie in the middle of the individual values, i.e. that the mean and the median coincide. If this is not the case then the following situations and corresponding causes may be distinguished:

a) One or more extreme values on the one side neutralize a larger number of opposed, more closely grouped, values. As figure 3 shows, this sampling situation can arise by the chance inclusion in the sample of rare though still normal extreme deviations among the population. Such extremes must be examined with a view to the possible participation of some non-fortuitous cause. If the latter is found to be the case, the extremes concerned must be omitted and the mean and variance recalculated without them. This procedure, however, is only necessary when a causal relationship between extreme value and origin has been demonstrated. In a blood-circulation study on healthy subjects, for example, an extreme may be found to be due to the inclusion, unknown to the investigator, of a heart-sufferer. If in a subsequent check an extreme were found in a vagotonic subject then omission of the value would only be justified if a fresh series of tests on vagotonics yielded results of the kind shown in figure 4:



The extremes in the test on healthy subjects would then be explicable as normal values for vagotonics, i.e. for a different population a' , reacting differently. This purely imaginary example shows how a statistical examination can bring new interrelationships to light (the example is merely illustrative, in reality the variations are rarely so pronounced).

If the examination of the extremes shows no evidence of non-fortuitous causes, then it is in order to omit them provided that they satisfy CHAUVENET's criterion (see page 47). However, since the limits of the latter were fixed in part by arbitrary considerations, it is more reliable, as far as evaluation of extremes is concerned, to repeat the test with a larger number of observations. In the elimination of extremes one should always bear in mind that the “wish as father to the thought” has often been the censor of “undesirable” values!

b) The distribution of the individual values does not always show such a pronounced one-sided grouping as in the above example. **Fig. 5***



In a distribution such as figure 5a it is impossible to decide, on the basis of a limited sample, whether or not it is fortuitous; only one or more repetitions can give the answer. If the repetitions show a tendency for the mean to approach the middle of the individual values, then the result of the original sample may be ascribed to chance. If the same picture is repeated however, it must be assumed that the values are being subjected to the influence of some extraneous factor. The origin may lie in a systematic error in the experiment such as would occur, for example, were blood-sugar determinations made between midday and 6 p.m. The blood sugar will be higher in subjects tested shortly after the midday meal than in those tested shortly before the evening meal. The fluctuating blood-sugar level inevitably affects the distribution, mean and variance of the sample. Investigations in which such a rhythmic influence is presumed to be present should accordingly be made either during as short a space of time as possible, or if this is impossible, at a predetermined time, e.g. daily between 8 a.m. and 9 a.m. Obviously the condition of the subject should be prescribed (fasting, replete, resting, etc.), although experience shows that this cannot be relied upon.

Such systematic influences cannot always be excluded experimentally, since they are frequently linked to functions partici-

* Fig. 5a: Individual values the logarithms of which are normally distributed.

Fig. 5b: Normal distribution of the logarithms of the values in figure 5a.

pating in the building-up of the population. If for example the weight increase of an animal proceeds in proportion to its body-weight, then it is more probable that chance will have a constant effect on the logarithm of the body-weight than on the body-weight itself. It is then the logarithm of the body-weight which is normally distributed, and not the body-weight itself¹. Nature measures with scales different to ours. Compared to our linear scale they are mostly of exponential form. An example is provided by the WEBER-FECHNER law, whereby a subjective sensation increases with the logarithm of the objective influence. The same holds good in toxicology, where the dosage must be increased exponentially in order to produce a linear increase in effect. In such

cases it is not the sample values but their logarithms which are normally distributed.

Distributions in which the logarithms of the individual values are normally distributed are known as *lognormal distributions*, and are of importance in biology. Examples are: effects of drugs and disinfectants; sensitivity threshold of the sense of touch when tested with very small weights; in blood²: urine, non-protein nitrogen, creatinine, cholesterol, potassium, bilirubin, phosphatides (inorganic P normal), acid-soluble phosphorus, acid and alkaline phosphatase, amylase, etc.

For variance of the means, see distribution of the means, page 38.

The binomial distribution

The binomial* or BERNOULLI distribution is a discrete distribution which finds application mainly in the statistics of events and in genetics.

If the occurrence of an event (e.g. throwing of a six with dice) is denoted by *p*, then clearly (1-*p*) is the probability of the non-occurrence of this event. The figure 1 denotes the total probability of the occurrence and non-occurrence of the event (multiplied by 100 = %). On the grounds of simplicity and logic the expression (1-*p*) is denoted by *q*, since in place of the non-occurrence of the *p*-event, e.g. in place of a boy, another event, a girl, could in certain circumstances occur. The important thing is

$$(p + q)^N = \binom{N}{0} p^N + \binom{N}{1} p^{N-1} q + \binom{N}{2} p^{N-2} q^2 + \dots + \binom{N}{N-1} p q^{N-1} + \binom{N}{N} q^N$$

$$\binom{N}{k}, \text{ read as } N \text{ over } k, \text{ is the abbreviation for the binomial coefficient } \frac{N!}{k!(N-k)!} \tag{4}$$

This is the formula by which the number of possible combinations of *N* characteristics in groups of *k* characteristics is calculated. The reader should not be deterred by this formula, since the desired result is achieved by means of the following:

- 1. The exclamation mark following *N* and *k* denotes the factorial = *N* × (*N* - 1) × (*N* - 2) × ... × 3 × 2 × 1.
- 4! for example means 4 × 3 × 2 × 1. Factorials of the numbers 1 to 100 can be read off from the table on page 24.

Example 2.

Terms numbered according to the exponent of p

$$(p + q)^6 = \frac{6!}{6!} p^6 + \frac{6!}{1!5!} p^5 q + \frac{6!}{2!4!} p^4 q^2 + \frac{6!}{3!3!} p^3 q^3 + \frac{6!}{4!2!} p^2 q^4 + \frac{6!}{5!1!} p q^5 + \frac{6!}{6!} q^6$$

The binomial coefficients for terms 6 and 0 are equal to 1, those for terms 1 to 5 can be calculated with the help of the table of factorials on page 24. It will be seen that terms 6, 5, 4 are of the same magnitude as terms 2, 1, 0, since *p* = *q* = 0.5. For the same reason also *p*⁶ = *p*⁵ *q* = *p*⁴ *q*², etc.

We thus obtain the binomial coefficients

6	5	4	3	2	1	0
1	6	15	20	15	6	1

which with the constant factor *p*⁶ = 0.015625 yield the following probability distribution :

Term	Probability**	Probability in %**	Significance		
6	0.015625	1.5625	(p ⁶)	boys?	girls?
5	0.093750	9.3750	(p ⁵ q)	all	and none
4	0.234375	23.4375	(p ⁴ q ²)	5 »	1
3	0.312500	31.2500	(p ³ q ³)	4 »	2
2	0.234375	23.4375	(p ² q ⁴)	3 »	3
1	0.093750	9.3750	(p q ⁵)	2 »	4
0	0.015625	1.5625	(q ⁶)	1 »	5
				none »	all
Total 1.000000 (for checking)		Total 100.0000 (for checking)	} in 6 births in one family, given a genetical proba- bility of 0.5 both for boys and for girls		

The following information can be obtained from this distribution: among six births, what is the probability of obtaining at least one boy? On summation of all the probabilities of the "boy-terms" (*p*-terms), or on subtracting the probability of the "girl-only" term from 1, we obtain the answer, 98.4375%. If we ask what is the probability of obtaining at least 2, 3 . . . boys, the answer is provided by summation of the probabilities of the *p*-terms 2, 3 . . . up to 6, or by summation of the opposite probabilities for girls from term 0 to term 6 and as before subtracting from 1 or 100. The probabilities for girls may be obtained analogously.

This distribution cannot, however, predict the subsequent probability of boy or girl when, say, 4 births have already occurred. This requires the further calculation of the binomial with *N* = 2. In addition, even were *p* genetically exactly equal to *q*, chance factors would result in deviations from this theoretical distribution. For a discussion on the fortuitous or other origin of deviations, see page 38 et seq.

¹) GADDUM, J. H., *Nature*, 156, 463, 1945. ²) WOOTTON and KING, *Lancet*, 1, 470, 1953.

* This is a special case of the multinomial $\frac{n!}{a_1! a_2! \dots a_r!} p_1^{a_1} p_2^{a_2} \dots p_r^{a_r}$, where *a*₁ = probability of occurrence of *p*₁, etc.

** In publishing statistical results, particularly with regard to events, which can obviously only occur integrally, there is naturally no point in giving decimal figures to many decimal places and as a rule one decimal place is ample. They are of course necessary in the course of the calculations for checking (sum of the probabilities = 1 or 100).

The mean and variance of the binomial distribution are given by the following formulae:

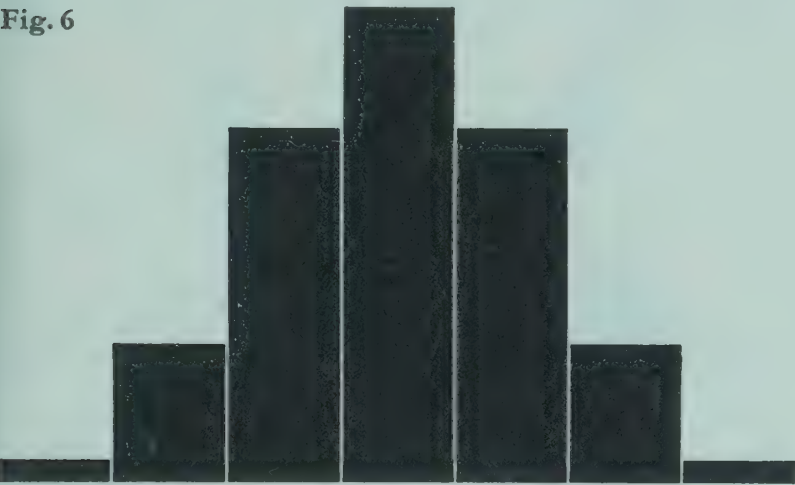
	Sample	Expressed as relative frequency
Mean	$\bar{x} = p \cdot N$ (5)	$m = p$ multiplied by 100 = % (7)
Variance	$s^2 = N \cdot p q$ (6)	$\sigma^2 = \frac{p q}{N}$ (8)
Standard deviation	$s = \sqrt{s^2}$	$\sigma = \sqrt{\sigma^2}$ multiplied by 100 = %

Example 3.
Of 60 tries, 40 are successful.
 $N = 60, p = \frac{40}{60}, q = 1 - \frac{40}{60}$

$$\bar{x} = \frac{40}{60} \times 60 = 40 \text{ (tries)}$$
$$s^2 = 60 \times \frac{40}{60} \left(1 - \frac{40}{60}\right) = 13.3$$
$$s = 3.6 \text{ (tries)}$$

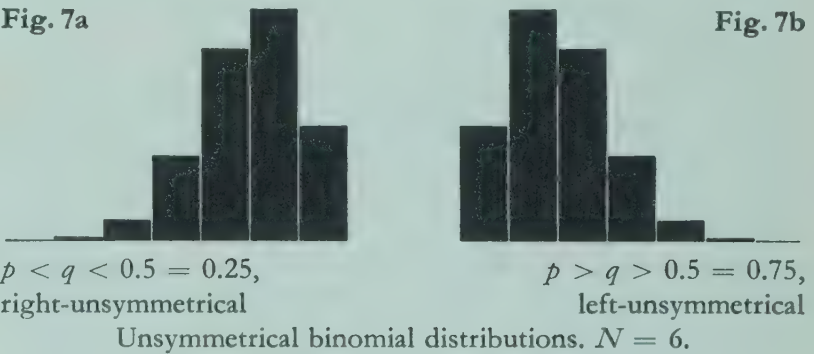
$$= \frac{40}{60} = 0.666\ldots \text{ or } 66.6 \%$$
$$= \frac{2}{9 \times 60} = 0.003704$$
$$= 0.061 \text{ or } 6.1 \%$$

Represented graphically, the binomial distribution described in example 2, with $N = 6$ and $p = q = 0.5$, has the following form:



Binomial distribution. $N = 6, p = q = 0.5$.

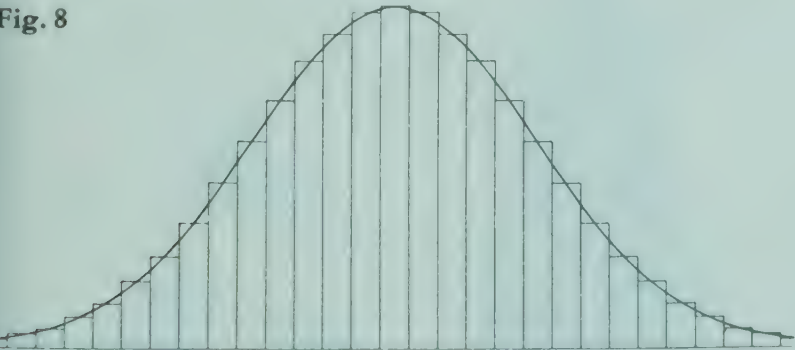
The distribution is symmetrical, but only as long as $p = 0.5$. If p increases, the distribution becomes left-unsymmetrical; if p decreases, it becomes right-unsymmetrical.



With a larger number N of tries the asymmetry of such distributions decreases, provided that p or q is not too small (does not tend towards zero). In practice it should be noted that the more p differs from 0.5, the greater N must be, if a symmetrical distribution is to be reckoned with. This is important inasmuch as the safety limits derived from the normal distribution are valid for binomial distributions only when the latter are more or less symmetrical. If p tends towards zero and N towards infinity, the distribution becomes a Poisson distribution of rare events. Since this distribution is of little importance in medicine it will not be discussed here. On the other hand, if we set $p = q = 0.5$ and let N tend towards infinity, the distribution becomes a normal distribution (GAUSS-LAPLACE distribution, GALTON distribution, distribution of errors, etc.).

The normal distribution

As the foregoing shows, this may be regarded as a limiting case of the binomial distribution. When N in figure 6 tends towards infinity the following result is obtained:

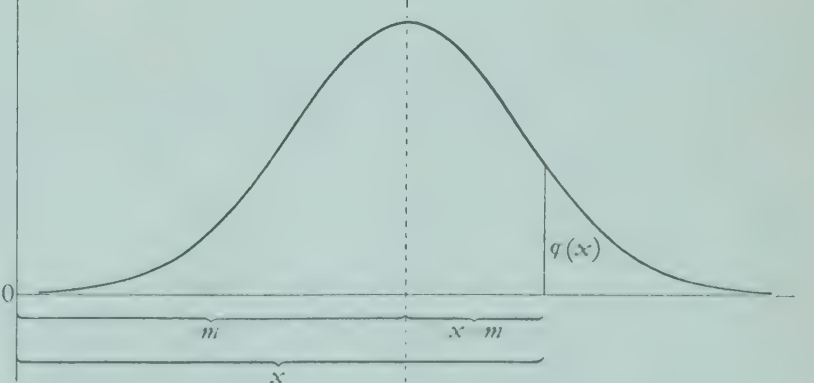


The individual probability rectangles becomes eventually infinitely thin, so that their upper limits form a continuous curve. Since the total probability of all possible events remains unchanged, the area under the curve likewise remains equivalent to unity.

The general form of the normal distribution is

$$\varphi(x) = \frac{1}{\sigma \sqrt{2 \pi}} e^{-\frac{1}{2} \left(\frac{x - m}{\sigma}\right)^2} \quad (9)$$

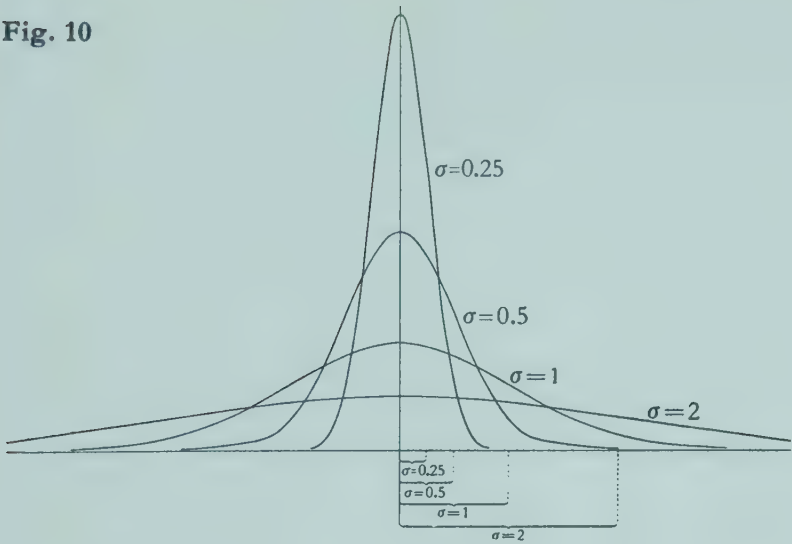
Fig. 9



- x = individual values
- m = mean
- $x - m$ = deviation from the mean
- σ = standard deviation = square root of the variance σ^2
- $\varphi(x)$ = probability of the point x
- e = base of natural logarithms = 2.718
- π = ratio of the circumference of a circle to its diameter = 3.14

The parameter m determines only the mean, i.e. the position of the curve with respect to the axis of ordinates. It has no effect on the shape of the curve, which is a function of the standard deviation σ , or square root of the variance σ^2 .

Fig. 10



A smaller standard deviation σ results in a steeper, narrower curve, a larger σ in a flatter curve.

The normal distribution symmetrical to the axis of ordinates is thus unequivocally characterized by the parameters mean and variance. The less a value deviates from the mean, the greater its probability. The probability of extreme deviations is indeed practically zero. Theoretically, too, negative values of x should occasionally occur, but this, naturally, can never be the case. In practice, however, this “anomaly” of the normal distribution is of no importance since deviations of, for example, 6σ occur in the normal distribution only once in 100 million cases.

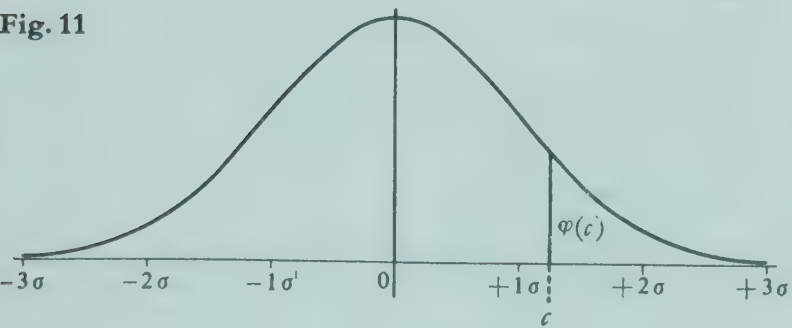
A further “weakness” of the normal distribution in the eyes of the non-mathematician is that the total probability 1 is represented by an area bounded on one side by a curve. It is therefore impossible to extract a single term, as in the case of the binomial distribution, and thereby calculate the probability of an event by means of simple rules. To do this, one must integrate between certain limits. This is unimportant in practice, since ordinates and areas of the normal distribution can be read from tables. This alleged “weakness” is in reality a great advantage since it means that the normal distribution can be applied to continuous distributions in which the deviations are not only by whole numbers but by any fractional number.

The **standard form** of the normal distribution on which the tables are based is obtained from by (9) setting $m = 0$ and $\sigma = 1$:

$$\varphi(c) = \frac{e^{-c^2/2}}{\sqrt{2\pi}} \tag{10}$$

$m = \text{zero}$
 $c = \text{deviation from the mean (zero)*}$
 $\sigma = 1 = \text{abscissa scale unit}$

Fig. 11



The general form is readily converted into the standard form by proceeding as follows: in the standard form the deviation c (since $\sigma = \text{abscissa unit} = 1$) is measured according to the standard deviation σ . If now the same is done in the general form, the deviation $(x - m)$ of the latter is converted into the corresponding deviation c of the standard form:

$$c = \frac{1}{\sigma} (x - m) \tag{11}$$

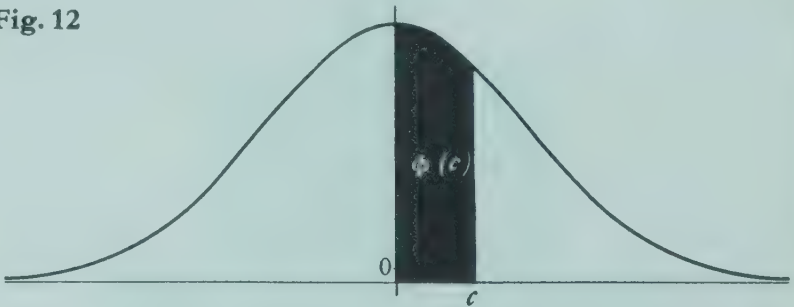
or vice versa

$$(x - m) = \sigma c, \text{ or } x = \sigma c + m \tag{12}$$

With the aid of equations 9, 10, 11, 12 the desired values, e.g. the corresponding normal distributions, the probabilities of certain deviations, etc., for any sample can be calculated by setting $m = \bar{x}$ and $\sigma = s^{**}$.

The area under the general (9) or standard (10) form of the normal distribution which embodies the integrated probability of all possible deviations, amounts as already mentioned to unity. The partial area $\Phi(c)$ above the deviation c now corresponds to the partial probability of all the deviations between the mean and c .

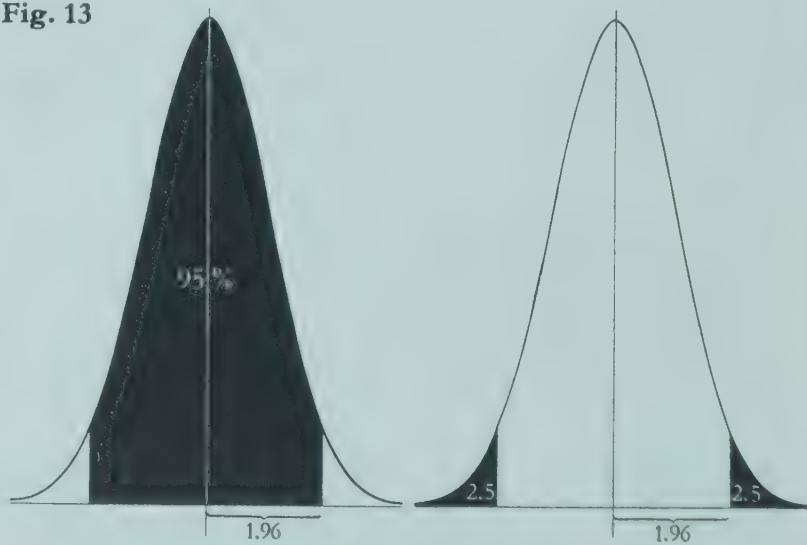
Fig. 12



Any possible partial probability can readily be calculated by means of tables. On the opposite page a number of problems of importance in practice have been summarized in tabular form, together with the appropriate solutions. Even the non-mathematician should find that these present little difficulty.

It is instructive to consider in more detail two of the determinations of areas listed in this table. When limits are drawn symmetrically above and below the mean, the following two questions arise: “What is the probability of the totality of all deviations *inside* or *outside* these limits?” These probabilities may be represented diagrammatically as follows (black areas = probabilities):

Fig. 13



(continued on page 38)

* Deviations are here denoted by the symbol c , but as multiples of σ they are usually denoted by t . The symbol c has been chosen in order to prevent the non-mathematician confusing it with the t -distribution.

** If, for example, the values of $\varphi(x)$ for any sample are calculated in accordance with formula (9) and with the aid of formula (11), it should be realized that the curve of relative frequencies (area = 1) is thereby obtained. To obtain the curve corresponding absolutely to the sample, the values of $\varphi(x)$ must be multiplied by the total number of observations N and the class width k .

$$\varphi(x)_{\text{absolute}} = k \times N \times \varphi(x)_{\text{relative}}$$

Calculation of Probability Ranges (Frequency Ranges) of the Normal Distribution
using the tables provided in the *GEIGY Scientific Tables*


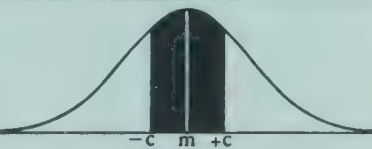

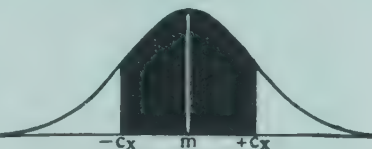

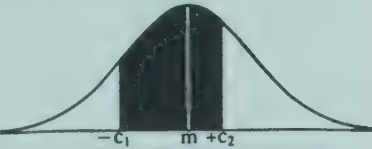

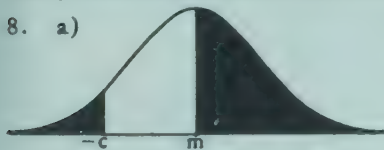


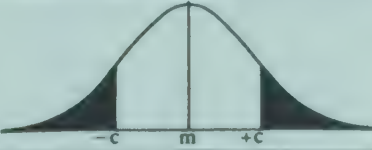
The probability ranges correspond to areas under the normal distribution inside or outside the ordinates of any normal deviation ϵ . The latter is obtained from any deviation $x - m$ or $x - \bar{x}$ by division by σ or s respectively.

$$\epsilon = \frac{x - m}{\sigma} \text{ or } \frac{x - \bar{x}}{s}$$

Conversely, any deviation $x - m$ or $x - \bar{x}$ is obtained from the normal deviation ϵ by multiplying by σ or s respectively.

$$\begin{aligned} x - m &= \sigma \epsilon & x - \bar{x} &= s \epsilon \\ \text{and} \quad x &= \sigma \epsilon + m & x &= s \epsilon + \bar{x} \end{aligned}$$

The areas in the tables (excepting the table of probits) are given in decimal fractions of the total area = 1. The corresponding frequency percentages are obtained by multiplying by 100, the absolute frequencies by multiplying by the total frequency N of any distribution.

A. Probability inside given limits			
Problem	Table	Entry at	Solution
<div>1.</div> <div></div> <div>Given the normal deviation $+\epsilon$ or $-\epsilon$. Required to find the probability of all deviations between the mean and $+\epsilon$ or between the mean and $-\epsilon$.</div>	page 25	ϵ	$\Phi(\epsilon)$, positive for $+\epsilon$ as well as $-\epsilon$.
<div>2.</div> <div></div> <div>Given the normal deviation ϵ. Required to find the probability of all deviations between the mean and $\pm \epsilon$.</div>	page 25	ϵ	$\Phi(\epsilon) \times 2$
<div>3.</div> <div></div> <div>Given the probability between the mean and the normal deviation ϵ_x. Required ϵ_x.</div>	page 27 Probits	% If not already expressed as %, the given probability is converted into % by multiplying by 100 and adding 50.	Probit - 5 = ϵ_x (plus or minus).
<div>4.</div> <div></div> <div>Given a probability located symmetrically above and below the mean. Required to find the corresponding limits ϵ_x.</div>	page 29 lower (Probability P)	P To obtain P , subtract the given probability from 1.	ϵ (plus or minus)
<div>5.</div> <div></div> <div>Given normal deviations $+\epsilon_1$ and $+\epsilon_2$ or $-\epsilon_1$ and $-\epsilon_2$ (ϵ_1 smaller than ϵ_2). Required to find the probability of all deviations between ϵ_1 and ϵ_2.</div>	page 25	$\begin{matrix} +\epsilon_1 \\ +\epsilon_2 \end{matrix} \left. \vphantom{\begin{matrix} +\epsilon_1 \\ +\epsilon_2 \end{matrix}} \right\} \dots\dots\dots$ $\begin{matrix} -\epsilon_1 \\ -\epsilon_2 \end{matrix} \left. \vphantom{\begin{matrix} -\epsilon_1 \\ -\epsilon_2 \end{matrix}} \right\} \dots\dots\dots$	$\Phi(\epsilon_2) - \Phi(\epsilon_1)$ $\Phi(\epsilon_2) - \Phi(\epsilon_1)$
<div>6.</div> <div></div> <div>Given the normal deviations $-\epsilon_1$ and $+\epsilon_2$. Required to find the probability of all deviations between $-\epsilon_1$ and $+\epsilon_2$.</div>	page 25	$\begin{matrix} -\epsilon_1 \\ +\epsilon_2 \end{matrix} \left. \vphantom{\begin{matrix} -\epsilon_1 \\ +\epsilon_2 \end{matrix}} \right\} \dots\dots\dots$	$\Phi(\epsilon_1) + \Phi(\epsilon_2)$
<div>7.</div> <div></div> <div>Given the normal deviation $-\epsilon$ or $+\epsilon$. Required to find the relative frequency of all deviations between $-\infty$ and $-\epsilon$ or between $-\infty$ and $+\epsilon$.</div>	page 27 Probits	Probits To obtain the probit, add 5 to the given deviation ϵ .	% (divided by 100 = probability)
B. Probability outside given limits			
Given the normal deviation $-\epsilon$ or $+\epsilon$. Required to find the probability (black areas) outside these limits in the following cases:			
<div>8. a)</div> <div></div> <div>b)</div> <div></div>	page 29 upper (Normal probability integral)	$\epsilon \dots\dots\dots \left\{ \begin{array}{l} \text{a) } 0.5 + \frac{1}{2} P \\ \text{b) } \frac{1}{2} P \end{array} \right.$	
<div>9.</div> <div></div>			
<div>10.</div> <div></div>	page 29 lower (Probability P)	P	ϵ (plus or minus)

Interpretations:

- a) Inside the limits mean $\pm c$ so many per cent of all chance deviations may be expected.
- b) The probability of a chance deviation $\pm c$ or larger amounts to so many per cent, i.e. in 100 cases so many per cent of chance deviations $\pm c$ or larger are to be expected. This is known as the **probability of the deviation c** and is given the symbol P .

All conclusions derived from the normal distribution are valid strictly for normally distributed populations only. Populations must therefore be tested for "normality", and in this connection the following should be borne in mind: small random samples (sample populations) are seldom normally distributed, even when the whole population is so distributed. It has already been shown that binomial distributions with p not equal to 0.5 are unsymmetrical with low values of N , i.e. they cannot be replaced by normal distributions. A test for normality is for this reason superfluous with small samples. The question "normal or not" can only be answered with certainty in the case of large samples. Tests for normality may be made in various ways, and descriptions of these will be found in the literature. The method of probits (see page 44) is very convenient for the less experienced.

If the test shows the population not to be normal, there are three possibilities to be considered:

1. The population is not homogeneous but is a combination, for example, of two normally distributed populations. The result is seen in curves which are unsymmetrical or have multiple peaks. Normalization can be achieved by improved methods of selection in building up the population.
2. The population is intrinsically normally distributed but has not been measured by means of an appropriate scale (cf. the section on mean and variance). A change in the x -scale (individual values), for example by logarithmic transformation, will here achieve normalization.
3. The population is definitely not normally distributed and cannot be normalized either by changing the method of selection or by changing the scale.

Distribution of means

If several samples from a population are taken, the means of these samples never coincide with the "true" mean of the population but are either greater or smaller, i.e. the sample means are distributed around the "true" mean.

The *variance of the mean* of a sample is

$$s_x^2 = \frac{1}{N} s^2 \tag{13}$$

and the *standard deviation of the mean*

$$s_x = \frac{1}{\sqrt{N}} s \tag{14}$$

where N is the total number of values of all the samples, and s^2 the variance of the sample.

The variance of the mean is thus smaller, the greater the number of individual values. Larger samples are therefore more reliable than small ones, provided that care is exercised in their make-up.

The means of larger samples are normally distributed, and this is also approximately so when the individual values themselves are not normally distributed. For this reason it is quite unnecessary to test the normality of distributions when only their means are to be compared.

The means of smaller samples on the other hand are no longer normally distributed, but follow the t -distribution of GOSSET ("Student"). The latter proposed a distribution very similar to the normal distribution but with a flatter curve, the variance being dependent only on the number of degrees of freedom n . This number in turn bears a definite relation to the number N of individual values.

In testing the deviation of means, or of differences of means, etc., the following should be noted:

- a) If the number of degrees of freedom n is greater than 60, then the distribution of the means follows the normal distribution (deviation c)*.
- b) If the number of degrees of freedom n is less than 60, then the distribution of the means follows the t -distribution (deviation t)*.

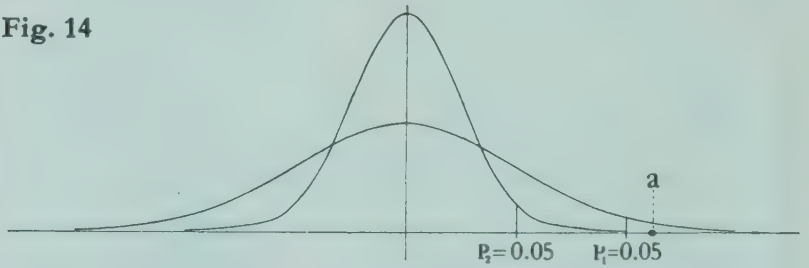
The determination of the number of degrees of freedom n will be discussed individually in dealing with the various problems which follow.

Statistical testing for chance or non-chance

In the normal distribution with standard deviation $\sigma = 1$, the probability P of the deviation $c = 1.96$, taken from the table on page 29, is 0.05, i.e. in 100 cases only 5 chance deviations of value ± 1.96 or greater can be expected. It can therefore be assumed, without a great degree of error, that a deviation from zero (= mean of the standard form of the normal distribution) greater than 1.96 is no longer fortuitous. For any deviation differing significantly from zero the value of P must be 0.05 or smaller.

The non-fortuitous nature of any deviation can thus be decided with a high degree of probability; the converse, i.e. the fortuitous nature of a deviation, can on the other hand never be decided with certainty. This is demonstrated by formula (14) in the previous section, whereby the standard deviation of the mean with increasing size of the sample decreases in proportion to the square root of the size of the sample. The distribution of the means of larger samples is thus narrower than that for smaller samples (cf. fig. 10, shape of the normal distribution for various standard deviations), while the infinitely large population has the smallest distribution. Figure 14 shows the distribution of a population and that of a sample. On the basis of the limiting value for the sample of $P = 0.05$, the point a is significantly non-fortuitous, as explained above. On the basis of the limiting value for the population of $P = 0.05$, this significance is even more marked.

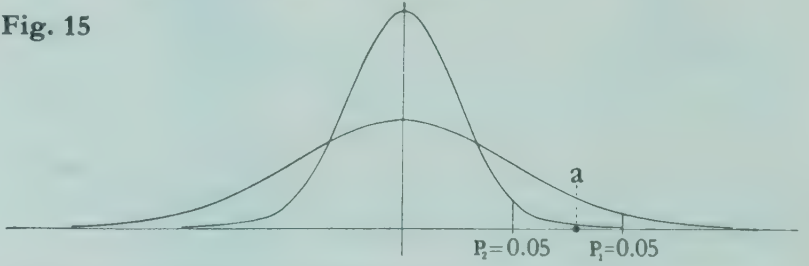
Fig. 14



Flatter curve = sample with limiting value P_1
Steeper curve = population with limiting value P_2

When the point a falls between the respective limits for population and sample, the position is different:

Fig. 15



Flatter curve = sample with limiting value P_1
Steeper curve = population with limiting value P_2

With respect to the population this value is significantly non-fortuitous, but with respect to the sample it is within the range of chance. This demonstrates clearly how unreliable a decision regarding the chance nature, i.e. the non-significance, of the deviation a would have been, had it been based on the evidence of the sample only. In testing the chance nature of small samples the following useful conclusions may thus be drawn:

1. In seeking to prove chance or non-chance (or, for example, agreement or non-agreement) always proceed with the object of proving the non-chance (the difference from zero, null-hypothesis).
2. If P is less than 0.05, the difference should be regarded as significant.
3. If P is greater than 0.05, it could be regarded as a case of chance

* Deviation c and corresponding P , see lower table on page 29. Deviation t and corresponding P , see upper table on page 30.

(or lack of difference, agreement), but the more cautious interpretation should be preferred.

4. The assumption should never be made that a difference is *not* significant.

Testing the significance of means

Whether a mean differs significantly from zero may be decided on the basis of the foregoing, as follows: given the sample (x), its mean \bar{x} and its variance s^2 and magnitude N , then the deviations c or t by means of which the probability P can be taken from the tables* are obtained from the following formula

$$c \text{ or } t = \frac{\bar{x}}{s_{\bar{x}}}, \text{ } s_{\bar{x}} \text{ from (14)} \tag{15}$$

degree of freedom $n = N - 1$ ($n > 60: c; n < 60: t$)

Example 4. It is desired to test the difference in effect of two soporifics, a and b. Both compounds are administered to the same five subjects and the duration of sleep recorded:

Soporific	a	b	(a - b) = (x)	(a - b) ² = (x ²)
Duration of sleep (subject 1)	8	12	— 4	16
(subject 2)	6	5	+ 1	1
(subject 3)	8	13	— 5	25
(subject 4)	6	10	— 4	16
(subject 5)	10	13	— 3	9
			S (x) — 15	S (x ²) 67, N = 5
Mean \bar{x}	= — 3			
Variance s^2	= 5.5			
Variance of the mean $s_{\bar{x}}^2$	= 1.1			
Standard deviation of the mean $s_{\bar{x}}$	= 1.049			
Degree of freedom $n = 4. t = \frac{3}{1.049}$	= 2.86			

The corresponding probability P (from the table on page 30) lies between 0.05 and 0.02. The mean of the duration differences thus differs significantly from zero, i.e. it is not fortuitous that the average duration of sleep due to one soporific is longer than that due to the other. In this case the two compounds have each been tested in turn on one subject. This is permissible provided that the two compounds are so administered that the first has no influence on the effect of the second. From the two distributions (a) and (b) a single distribution (a-b) has been built up from the differences in duration of sleep shown by each subject. This is justified as long as the two distributions are linked, as in this case, to one population group. It would not be justified if the two sample populations were based on two different population groups, i.e. if soporific a had been tested on 5 subjects and soporific b on 5 different subjects. In this latter case it would be necessary to test not the significance of a mean of differences but the significance of a difference of two means, as will be shown in the next section. There it will be seen that in such circumstances the difference in the efficacy of the two soporifics could not have been decided. The fundamental reason for this is that samples linked to a single population group are more markedly homogeneous. Wherever it is permissible and practicable it is therefore advisable, and more economical, to plan tests in this way.

Testing the significance of the difference of two means

The testing of the significance of the **difference** of two means is in principle the same as the testing of the significance of **one** mean. The deviations c or t by means of which the probability P is obtained are calculated by dividing the difference ($\bar{x} - \bar{x}'$) of the means by the standard deviation s_D of the difference of the means:

$$c \text{ or } t = \frac{\bar{x} - \bar{x}'}{s_D} \tag{16}$$

degree of freedom $n = N + N' - 2$

The standard deviation s_D of the difference of the means is calculated for large and small samples in *different* ways. For **large**

samples, i.e. where the degree of freedom n ($= N + N' - 2$) is greater than 60

$$s_D = \sqrt{s_x^2 + s_{x'}^2}; \text{ } s_x^2 \text{ and } s_{x'}^2, \text{ from (13)} \tag{17}$$

For **small** samples, i.e. where the degree of freedom n ($= N + N' - 2$) is less than 60, the two samples are combined and the *common* variance calculated as

$$s_{x, x'}^2 = \frac{S(x^2) - \bar{x} S(x) + S(x'^2) - \bar{x}' S(x')}{N + N' - 2} \tag{18}$$

Analogously to (13) and (17), the standard deviation of the difference of the means of small samples

$$s_D = \sqrt{\frac{s_{x, x'}^2}{N} + \frac{s_{x, x'}^2}{N'}} \tag{19}$$

or
$$= s_{x, x'} \sqrt{\frac{N + N'}{N N'}}$$

When only the parameters of small samples are known, the appropriate s_D cannot be calculated from (18) and (19), and formula (17) must be used.

Example 5. It is desired to test the difference in effect of two soporifics a and b ($= x$ and x'). The two compounds are administered each to a different group of five subjects. The durations of sleep are the same as in example 4.

Soporific	x	x ²	x'	x' ²
Duration of sleep	8	64	12	144
	6	36	5	25
	8	64	13	169
	6	36	10	100
	10	100	13	169
	S (x) 38	S (x ²) 300	S (x') 53	S (x' ²) 607
Mean	$\bar{x} = 7.6$		$\bar{x}' = 10.6$	

Variance of the two samples (from 18)

$$s_{x, x'}^2 = \frac{300 - 288.8 + 607 - 561.8}{5 + 5 - 2} = 7.05$$

Standard deviation of the difference of the means (from 19)

$$s_D = \sqrt{\frac{7.05}{5} + \frac{7.05}{5}} = \sqrt{2.82} = 1.6793$$

and
$$t = \frac{7.6 - 10.6}{1.6793} = -1.78647$$

degree of freedom $n = 5 + 5 - 2 = 8$.

Since the corresponding probability P lies between 0.1 and 0.2, the difference of the means, i.e. the difference in effect of the two soporifics, can only be ascribed to chance.

A word concerning the difference of the means: it is absolutely irrelevant which mean is subtracted from which, since the difference is always taken as positive (symmetry of the normal deviation - the probability P for a negative deviation is the same as that for a positive one of the same magnitude).

Comparison of samples with the aid of the χ^2 -distribution

This test distribution, due to PEARSON, is eminently suitable when it is desired to compare observations (samples) with hypothetical values (anticipated values). It permits simultaneous comparison, class to class, of several distributions.

If the observed frequencies in each class amount to ($x + m$) and the hypothetical anticipated values to m , then

$$\chi^2 = S \left(\frac{x^2}{m} \right); x = (x + m) - m \tag{20}$$

* Deviation c and corresponding P , see lower table on page 29. Deviation t and corresponding P , see upper table on page 30.

From this general formula the value of χ^2 with summation over all the classes is obtained. With this value the probability P is taken from the table on page 30, with entry at the degree of freedom n . If P is less than 0.05 (or 0.01), then the difference between sample and anticipated values (expected distribution on the basis of the hypothesis) is significant. With higher values of P , from 10–90%, it is permissible to assume a certain agreement between the values compared, i.e. to regard the deviations between them as due to chance. Very high values of P , however, should be regarded with suspicion as being due to an error in calculation or a combination of extreme chances. Such a high degree of agreement is never as reliable as a more moderate one.

In working with the χ^2 -distribution the following special points should be noted:

- 1. Only frequencies (events) are compared, i.e. discrete values. χ^2 can also be applied, however, to continuous distributions,

provided that the individual values are in classes, or can be separated into classes: only frequencies are then taken into account, i.e. occupation of the classes, or likewise “events”.

- 2. Only corresponding classes may be compared with one another, i.e. the class width and class position must correspond.
- 3. The number of classes compared n' and the range of sample and expected distribution must agree. If this is not the case, then the range of the latter must always be made to agree with that of the former. In this case one should always proceed from the total range of the sample and omit the conversion to relative frequencies (total range 1 or 100).
- 4. The anticipated values (m) in any class of the *expected distribution* must not fall below 5. If this does occur, then a sufficiently occupied class can be created by combining a number of neighbouring classes. The corresponding classes of the sample must of course be likewise combined.

Example 6.

cm	1	2	3	4	5	6	7	8	9	10	11	
Given the sample ($x + m$)	1	2	8	25	33	45	38	20	6	3	0	$N_1 = 181$
Expected distribution (m)	0	1	5	23	35	40	35	23	5	1	0	$N_2 = 168$

The range N_2 of the expected distribution is first of all made to agree with the range N_1 of the sample by multiplying each class in (m) by 1.07738 ($= N_1/N_2$), giving the expected distribution

	0	1.08	5.38	24.78	37.71	43.09	37.71	24.78	5.38	1.08	0	$N_2 = 180.99$
--	---	------	------	-------	-------	-------	-------	-------	------	------	---	----------------

Since classes 1, 2 and 3 as well as 9, 10 and 11 of the expected distribution are occupied by less than 5 values, the first three and the last three classes of both distributions are combined, giving the following result for calculation of χ^2 :

Sample ($x + m$)	11	25	33	45	38	20	9	$N_1 = 181$	$n' = 7$
Expected distribution (m)	6.46	24.78	37.71	43.09	37.71	24.78	6.46	$N_2 = 180.99$	(n' = number of classes to be compared)

Now from (20) $x = (x + m) - m$: (11 – 6.46) (25 – 24.78) (33 – 37.71) etc.

and further from (20)

$$\chi^2 = \frac{(11 - 6.46)^2}{6.46} + \frac{(25 - 24.78)^2}{24.78} + \frac{(33 - 37.71)^2}{37.71} + \text{etc.}$$
$$\chi^2 = 5.807$$

In this case the degree of freedom n of χ^2 is determined as follows: the range N_2 of the expected distribution (m) is fixed by the range N_1 of the sample ($x + m$). The expected distribution therefore has no degree of freedom, while the sample has the degree of freedom $n = n' - 1$, where n' is the number of classes of the sample to be compared. In this example the degree of freedom for χ^2 is thus $n = 6$, giving a value of P from the table on page 30 between 0.50 and 0.30. The difference between sample and anticipated values (or between experiment and hypothesis) could therefore be due to chance.

Had the expected distribution in this example been calculated from the variance and mean of the sample, then the degree of freedom of χ^2 would have been ($n' - 2$), where n' is again the number of classes of the sample.

In comparing samples with anticipated values the following three initial situations may be distinguished:

- a) A sample is to be compared with a hypothetical distribution (e.g. binomial distribution, normal distribution, or any other curve, such as a parabola) which can be calculated by means of a known function. In this case the expected distribution (anticipated

values) is calculated from the total frequency of the sample. *The degree of freedom is obtained as in the above example.*

- b) A smaller sample is to be compared with a very large sample as expected distribution. The latter is again calculated as in a) from the range of the smaller sample. *The degree of freedom is obtained as in the above example.*

- c) It is desired to establish simply the differences between two or more samples, whereby the anticipated values can only be calculated from the samples. In this case a population based on the total of all sample frequencies is constructed by summation of the corresponding sample classes, and the expected distribution for comparison calculated from it.

In this case the degree of freedom n for χ^2 is calculated as

$$n = (n' - 1) (V - 1) \tag{21}$$

where n' is again the number of classes in a sample, V the number of samples to be compared (the calculated distributions of the anticipated values do not count in the determination of degree of freedom).

Examples of situation c).

A comparison of several samples will first be worked out, followed by several special cases of 2×2 and $2 \times n'$ tables.

Example 7. The frequencies of the hair colours fair, brown and black in boys and in girls have been counted in two parallel series of observations. It is desired to establish whether there is a significant sex difference in the distribution of these hair colours.

			fair	brown	black	total	
Sample series I	boys	(1)	30	105	46	181 = N_1	2 series of samples, total 4 samples
	girls	(2)	28	122	50	200 = N_2	
Sample series II	boys	(3)	68	155	81	304 = N_3	
	girls	(4)	72	180	99	351 = N_4	
Total			198 = N'	562 = N''	276 = N'''	1036 = N	

The required reduced population is given in the bottom line of this table. In it there is no distinction between boys and girls. From the individual classes of this population the anticipated values are now calculated in proportion to the totals of the samples (extreme right-hand column). These anticipated values are based

The anticipated values (m) are calculated as follows:

for boys (1) fair = $\frac{N_1}{N} N' = \frac{181}{1036} 198 = 34.59$; boys (1) brown = $\frac{N_1}{N} N'' = \frac{181}{1036} 562 = 98.18$; etc.
or
for girls (4) fair = $\frac{N_4}{N} N' = \frac{351}{1036} 198 = 67.08$; girls (4) brown = $\frac{N_4}{N} N'' = \frac{351}{1036} 562 = 190.41$; etc.

We now obtain (anticipated values in brackets)				fair	brown	black	total	
Series I	{	boys	(1)	$(m + x)$ (m)	30 (34.59)	105 (98.18)	46 (48.22)	181 (180.99)
		girls	(2)	$(m + x)$ (m)	28 (38.21)	122 (108.47)	50 (53.27)	200 (199.95)
Series II	{	boys	(3)	$(m + x)$ (m)	68 (58.09)	155 (164.89)	81 (80.98)	304 (303.96)
		girls	(4)	$(m + x)$ (m)	72 (67.08)	180 (190.41)	99 (93.51)	351 (351)
Total				$(m + x)$ (m)	198 (197.97)	562 (561.95)	276 (275.98)	1036 (1035.90)

Tests: The sum of the anticipated values of the individual classes (columns) must be equal to the sum of the corresponding sample values.
The sum of the anticipated values in each line must be likewise equal to the sum of the corresponding sample values.
The sum of the totals in the last column must be equal to the sum of the totals in the bottom line.

From (20) the separate components of χ^2 are now calculated from the sample values and corresponding anticipated values:

		fair	brown	black
boys	(1)	0.60908	0.47375	0.10220
girls	(2)	2.72819	1.68766	0.20073
boys	(3)	1.69062	0.59319	0.00005
girls	(4)	0.36086	0.56913	0.32232
		$\chi^2 = 9.33778$		

The degree of freedom from (21) is $(3 - 1) (4 - 1) = 6$. Entry with this n for $\chi^2 = 9.338$ gives P between 0.1 and 0.2, so that the sex difference with regard to hair colour could be due to chance.

Comparisons of two samples with two or more classes are more frequent than comparisons such as the above of several samples with several classes. As a result of their presentation in tabular form, these are known as 2×2 and $2 \times n'$ tables respectively.

A 2×2 table arises with the following problem, very often encountered in medical practice:

Example 8.

Of 108 subjects treated prophylactically with a drug, 20 became ill; of 237 controls given placebos, 74 became ill. Is there a significant difference in effect between drug and placebo?

The appropriate 2×2 table is constructed

	Affected		Unaffected		Total
Drug	(a)	20	(c)	88	(e) 108
Placebo	(b)	74	(d)	163	(f) 237
Total	(g)	94	(h)	251	(i) 345

on the hypothesis that there is no difference between boys and girls (null hypothesis). If now samples and anticipated values show a difference with a low value of P , then the sex difference in the distribution of these hair colours may be regarded as significant. When otherwise, the deviation can be due to chance.

The bottom line again represents the required reduced population in which there is no distinction between drug and placebo. The anticipated values are now calculated in a manner analogous to that in the hair-colour example. The process is, however, much simpler, since in a 2×2 table it is only necessary to calculate one of the anticipated values, e.g. (a), by multiplication and division:

$$a = \frac{g \times e}{i} = \frac{94 \times 108}{345} = 29.43 = m_a$$

All the other values are then obtained by simple subtraction from the totals. We now obtain (anticipated values in brackets)

	Affected		Unaffected		Total
Drug	(a)	20 (29.43)	(c)	88 (78.57)	(e) 108 (108)
Placebo	(b)	74 (64.57)	(d)	163 (172.43)	(f) 237 (237)
Total	(g)	94 (94)	(h)	251 (251)	(i) 345 (345)

x or x^2 is now obtained in the manner already described, whence it will be seen at once that in a 2×2 table all four values of x or x^2 are of the same magnitude. It is therefore simply necessary to calculate x^2 once, and to divide this figure by the four anticipated values.

We obtain $\chi^2 = 3.0216 + 1.3772 + 1.1318 + 0.5157 = 6.0463$.

Since there are two sample series each with two classes, in accordance with (21) $n = (2 - 1) (2 - 1) = 1$.

The degree of freedom n of any 2×2 table is equal to 1.

In this example, for $n = 1$ and $\chi^2 = 6.046$ a value of P between 0.02 and 0.01 is obtained, i.e. the difference between drug and placebo or between treated and untreated subjects is significant.

The following formula for 2×2 and also $2 \times n'$ tables enables quicker calculations to be made (particularly with calculating machines):

					Total
Sample 1 ($a_1, a_2, a_3 \dots a_{n'}$)	a_1	a_2	a_3	S (a) = n_a
Sample 2 ($b_1, b_2, b_3 \dots b_{n'}$)	b_1	b_2	b_3	S (b) = n_b
Total	$a_1 + b_1$	$a_2 + b_2$	$a_3 + b_3$	S (a + b) = $n_a + n_b$
whence the quotients	$p_1 = \frac{a_1}{a_1 + b_1}$	$p_2 = \frac{a_2}{a_2 + b_2}$	$p_3 = \frac{a_3}{a_3 + b_3}$	$\bar{p} = \frac{n_a}{n_a + n_b}$; $\bar{q} = 1 - \bar{p}$
which with the products	$a_1 p_1$	$a_2 p_2$	$a_3 p_3$	$n_a \bar{p}$
yield	$\chi^2 = \frac{1}{p \bar{q}} [S (a p) - n_a \bar{p}]$				(22)
	Degree of freedom n (from 21) = $n' - 1$.				

In using this method the calculations should be taken to 5 decimal places in order to obtain χ^2 exactly to 2 decimal places.

Calculation of the above placebo example by this method yields

$$p_1 = 0.2127660 \quad p_2 = 0.3505976$$
$$a_1 p_1 = 4.2553200 \quad a_2 p_2 = 30.8525888$$
$$S(a p) - n_a \bar{p} = 1.2992108 \quad S(a p) = a_1 p_1 + a_2 p_2 = 35.1079088$$
$$\chi^2 = 6.04$$
$$\bar{p} = 0.3130435; \quad \bar{q} = 0.6869565; \quad \bar{p}\bar{q} = 0.2150473$$
$$n_a \bar{p} = 33.8086980$$

Examination of data by means of the χ^2 -formulae described is not possible for samples with classes of unequal size, or when only the parameters of the samples (cf. the literature) are known, or when the samples result from different experimental methods and cannot be directly compared. Such samples can nevertheless be compared with the aid of χ^2 by means of their probabilities P . The latter will be already known or can be calculated from the mean and variance. The appropriate values of χ^2 for the probabilities P to be compared are given by the formula

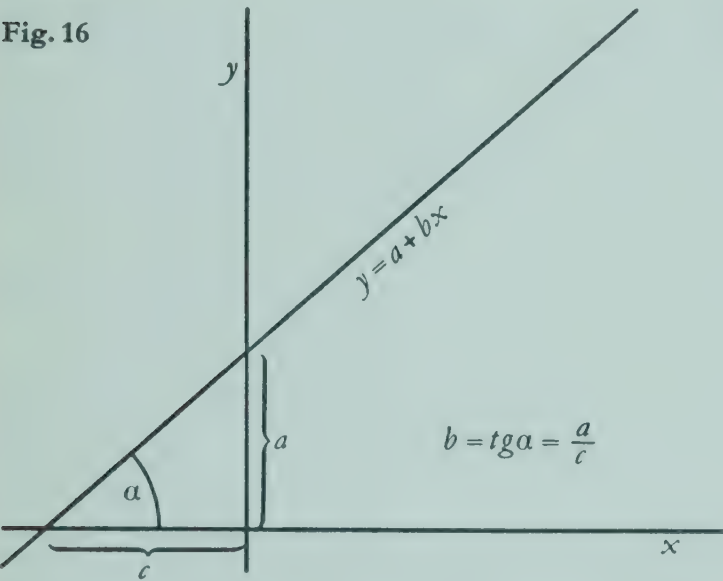
$$\chi^2 = -2 \times S(\log_e P) = -4.6052 \times S(\log_{10} P); \quad (23)$$

the degree of freedom n is equal to the number P multiplied by 2.

Regression, correlation

When the function $y = a + b x$ is plotted, a straight line is obtained.

Fig. 16



If now x is a magnitude subject to chance variations, this straight line becomes a swarm of points, the width of the swarm being determined by the variance of the variable x .

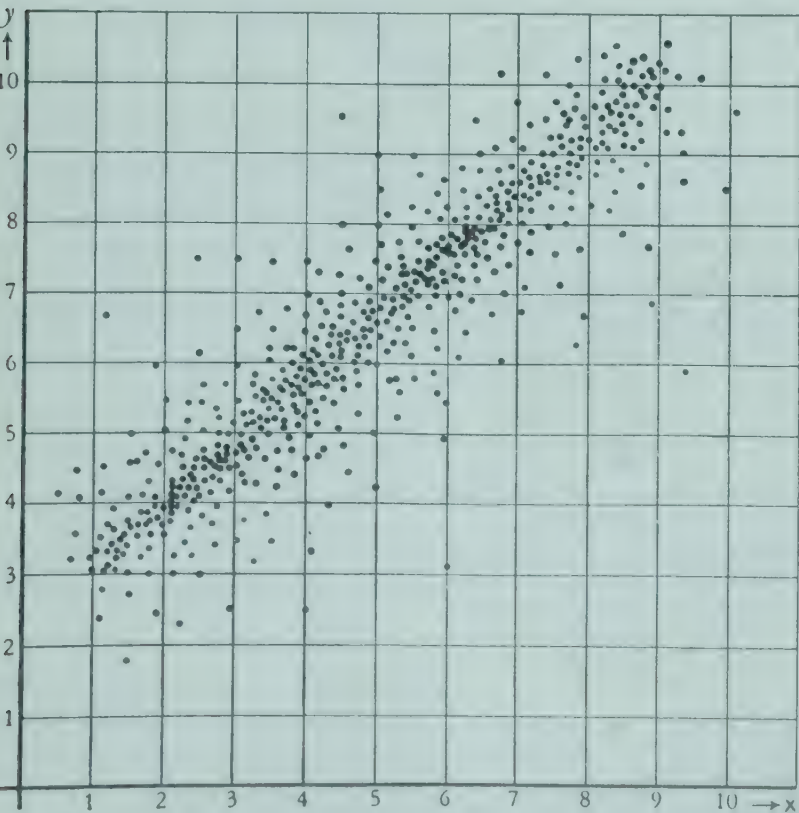


Fig. 17

If now y is likewise subject to chance variations the swarm of points will become still wider. According to whether y or x is regarded as the independent variable (from the purely mathematical standpoint) so will one or other of the following diagrams result:

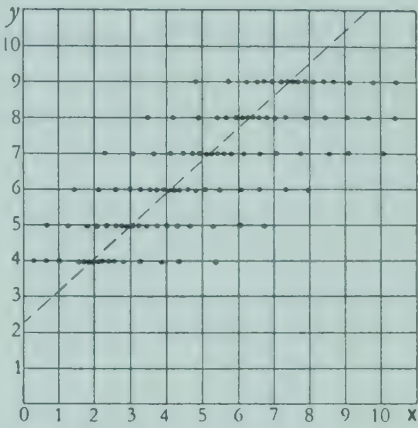


Fig. 18a Regression y to x

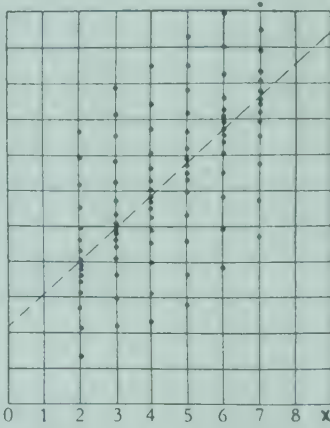
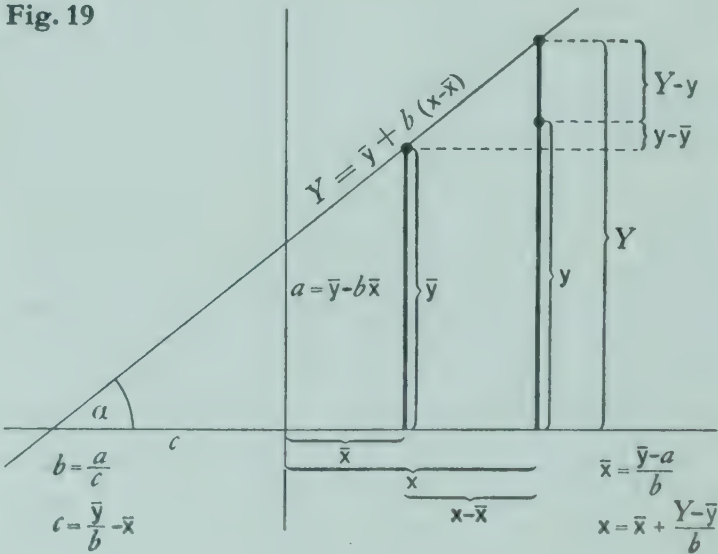


Fig. 18b Regression x to y

In these diagrams will be seen the familiar picture of normally distributed values. The combination of the means of these (actually an infinite number of normal distributions) constitutes a line known as the regression line. The corresponding function is known as the regression function.

Regression functions can be either linear or of higher form. By changing the x or y scale non-linear functions are always converted, where possible, to linear ones (cf. probit transformations for example) since the mathematical treatment of the latter is much simpler.

Fig. 19



The formulae for the linear regression y to x are: Given n' sample pairs x, y ; then the parameter a of the regression line

$$Y = a + b x \quad (24)$$

is

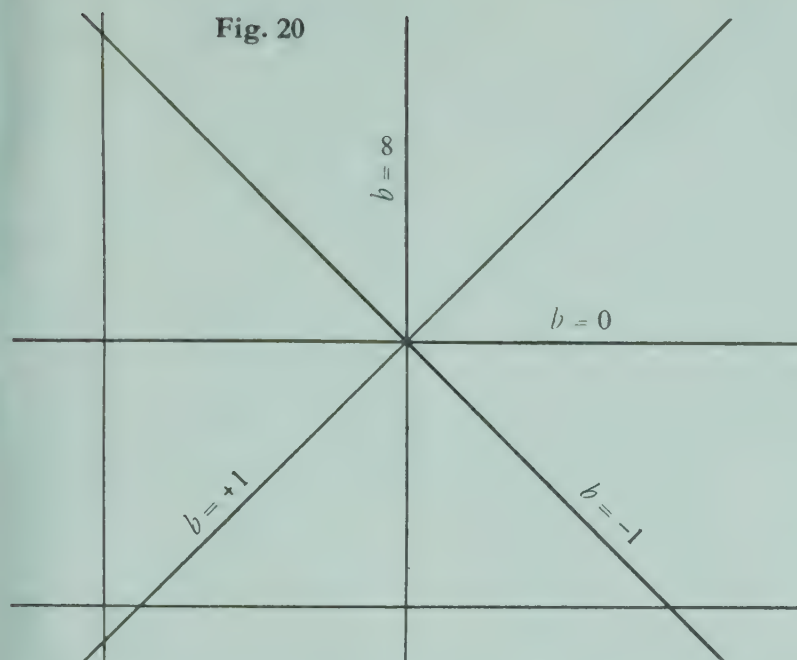
$$a = \bar{y} - b \bar{x} \quad (25)$$

Substituting (25) in (24) yields the usual form of the regression equation

$$Y = \bar{y} + b(x - \bar{x}) \quad (26)$$

The gradient b , known as the regression coefficient, is the tangent of the angle α between the regression line and the abscissa. It can be either positive or negative, the regression line then being either right or left inclined.

Fig. 20



The gradient b shows how many times y is smaller or greater (on the average) than x . It is calculated by dividing the covariance of the product xy by the variance of the individual values x .

The covariance xy is

$$s_{xy} = \frac{S(xy) - \bar{y} S(x)}{n' - 1} \quad (27)$$

the variance of x is

$$s_x^2 = \frac{S(x^2) - \bar{x} S(x)}{n' - 1} \quad (\text{formula 2b on page 32})$$

whence the regression coefficient b is given by

$$b = \frac{s_{xy}}{s_x^2} = \frac{S(xy) - \bar{y} S(x)}{S(x^2) - \bar{x} S(x)} \quad (28)$$

The denominator in formula (28) can be simplified in those cases where there is only one value of y for each value of x , and where the latter always increase by one unit, e.g.

x (weeks)	y (weight)
1	5.2
2	5.8
3	6.5
etc.	

It then becomes

$$S(x^2) - \bar{x} S(x) = \frac{1}{12} n' (n'^2 - 1) \quad (29)$$

The above formulae relate to the general and common regression of y to x , where y is the *dependent* and x the *independent* variable. In their practical application it is necessary to ensure that the physiologically dependent variable is taken as y and the independent (determinative) as x . The following are examples:

independent	dependent
x	y
Stature	Body-weight, body-surface, chest measurement, etc.
Body-weight, etc. of parents	Body-weight, etc. of children
Dosage	Gain in weight, blood levels, mortality rate, etc.

The opposite regression, x to y , gives as a rule a regression line somewhat differently inclined to that of the regression y to x (the usual). A measure of the mutual behaviour of these two lines is given by the **correlation coefficient** r . This is the geometrical mean of the two regression coefficients

$$b_{xy} = \frac{s_{xy}}{s_x^2} \quad (\text{the usual}) \quad \text{and} \quad b_{yx} = \frac{s_{xy}}{s_y^2}$$

$$r = \frac{s_{xy}}{\sqrt{s_x^2 s_y^2}} = \frac{s_{xy}}{s_x s_y} \quad (30)$$

The relation between the regression coefficient b_{xy} (here denoted simply by b) and the correlation coefficient r is given by

$$b = r \frac{s_y}{s_x}; \quad r = b \frac{s_x}{s_y} \quad (31, 32)$$

The square of the correlation coefficient, r^2 , is known as the *measure of certainty* and shows to what extent the independent variable x influences the dependent variable y . A measure of certainty of 0.5 for example indicates that 50% of the changes in y can be explained as due to changes in x – mathematically speaking. There is, however, no actual proof that the connection is a causal one, and the result should be regarded only as a pointer to the direction in which further investigation may yield direct proof. The same reservation applies also to the correlation.

The measure of certainty can have values between zero and 1, the correlation coefficient values between -1 and $+1$. A correlation coefficient of $+1$ or -1 indicates complete linear dependence (mathematical) whereby y increases or decreases respectively with increasing x .

The **significance test** of a *single* regression coefficient or correlation coefficient is similar in principle to that of a mean. The deviations c or t are calculated and thence the corresponding probability P . The deviations c or t are obtained from the following formulae:

Regression coefficient b .

$$c \text{ or } t = \frac{b}{s_b} \quad (33)$$

Degree of freedom $n = n' - 2$

In order to calculate the standard deviation s_b , the variance s_y^2 of all deviations $(y - Y)$ is first found:

$$s_y^2 = \frac{S(y - Y)^2}{n' - 2} \quad (34)$$

$$\text{where } S(y - Y)^2 = S(y^2) - \bar{y} S(y) - b^2 [S(x^2) - \bar{x} S(x)] \quad (35)$$

The standard deviation s_b is then

$$s_b = \frac{s_y}{\sqrt{S(x^2) - \bar{x} S(x)}} \quad (36)$$

Correlation coefficient r .

$$c \text{ or } t = \frac{r}{s_r} \quad (37)$$

Degree of freedom $n = n' - 2$

With larger samples ($n = n' - 2$, greater than 60; deviation c) the standard deviation s_r is

$$s_r = \frac{1 - r^2}{\sqrt{n' - 1}} \quad (38)$$

and with smaller samples (n less than 60; deviation t)

$$s_r = \sqrt{\frac{1 - r^2}{n' - 2}} \quad (39)$$

The **significance test of the difference** between *two* regression or correlation coefficients proceeds as follows:

Difference between two regression coefficients ($b - b'$) of two regressions Y and Y' with the pairs of values n' and n'' :

$$c \text{ or } t = \frac{b - b'}{s_{Db}} \quad (40)$$

Degree of freedom $n = n' + n'' - 4$

To calculate the standard deviation s_{Db} , the total variance $s_{Y, Y'}^2$ of all pairs of values $(y - Y)$ and $(y' - Y')$ of the two regression lines Y and Y' is first obtained:

$$s_{Y, Y'}^2 = \frac{S(y - Y)^2 + S(y' - Y')^2}{n' + n'' - 4} \quad (41)$$

whereby $S(y - Y)$ and $S(y' - Y')$ are calculated from (35).

Thence are obtained the variances

$$s_b^2 = \frac{s_{Y, Y'}^2}{S(x^2) - \bar{x} S(x)} \quad (42)$$

$$\text{and } s_{b'}^2 = \frac{s_{Y, Y'}^2}{S(x'^2) - \bar{x}' S(x')} \quad (43)$$

The standard deviation s_{Db} is then

$$s_{Db} = \sqrt{s_b^2 + s_{b'}^2} \quad (44)$$

With the difference of the correlation coefficients ($r - r'$), where the degree of freedom $n = n' + n'' - 4$ is greater than 60, the deviation c is

$$c = \frac{r - r'}{\sqrt{s_r^2 + s_{r'}^2}} \tag{45}$$

whereby $s_r^2 = \frac{(1 - r)^2}{n' - 1}$ (46)

and $s_{r'}^2 = \frac{(1 - r')^2}{n'' - 1}$ (47)

With a degree of freedom less than 60, the following conversion must be made:

namely $z = \frac{1}{2} \left(\log_e (1 + r) - \log_e (1 - r) \right) = 1.1513 \left(\log_{10} (1 + r) - \log_{10} (1 - r) \right)$ (48a)

and $z' = 1.1513 \left(\log_{10} (1 + r') - \log_{10} (1 - r') \right)$ (48b)

The variance of z is then

$$s_z^2 = \frac{1}{n' - 3} \quad \text{or} \quad s_{z'}^2 = \frac{1}{n'' - 3} \tag{49}$$

The value of P for the significance of the difference of two correlation coefficients, when n is less than 60, is then obtained on the basis of the normal deviation (not t) from

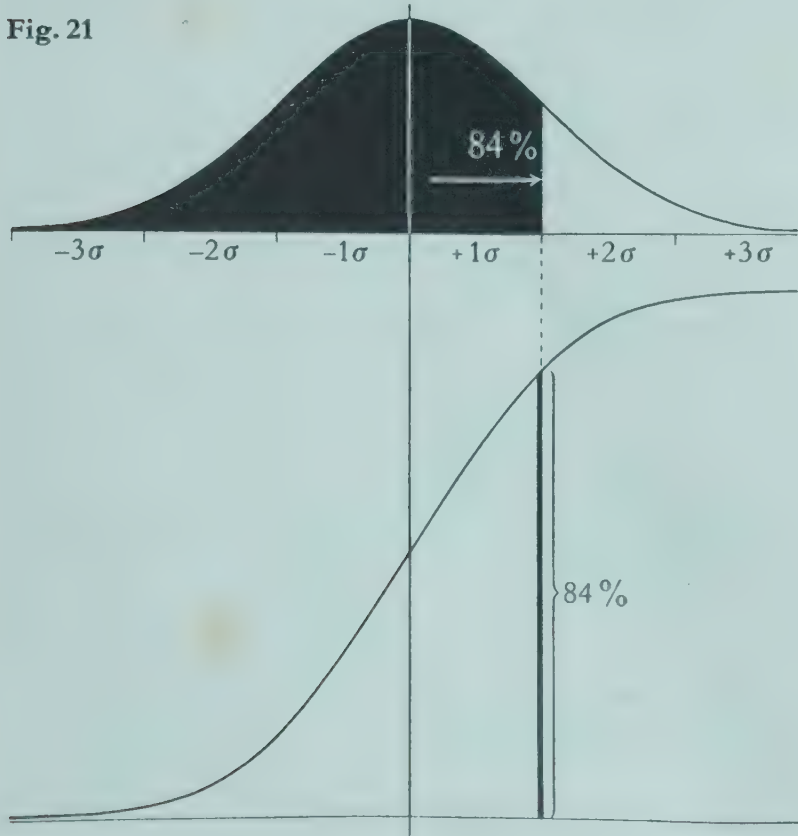
$$c = \frac{z - z'}{\sqrt{\frac{1}{n' - 3} + \frac{1}{n'' - 3}}} \tag{50}$$

The probit transformation

The probit transformation finds application mainly in the determination of the 50% lethal dose and similar dosage problems. It is useful in all those cases where a distribution must be tested for normality, or where the parameters of a population must be determined as exactly as possible from a few values which are known to have originated from a normally distributed population.

Continuous summation (from left to right) of the area under the normal distribution and plotting of the areas thus obtained as ordinates against a linear abscissa scale yields the so-called *sigmoid curve*. The values of its *ordinates* correspond to the *areas* of the normal distribution.

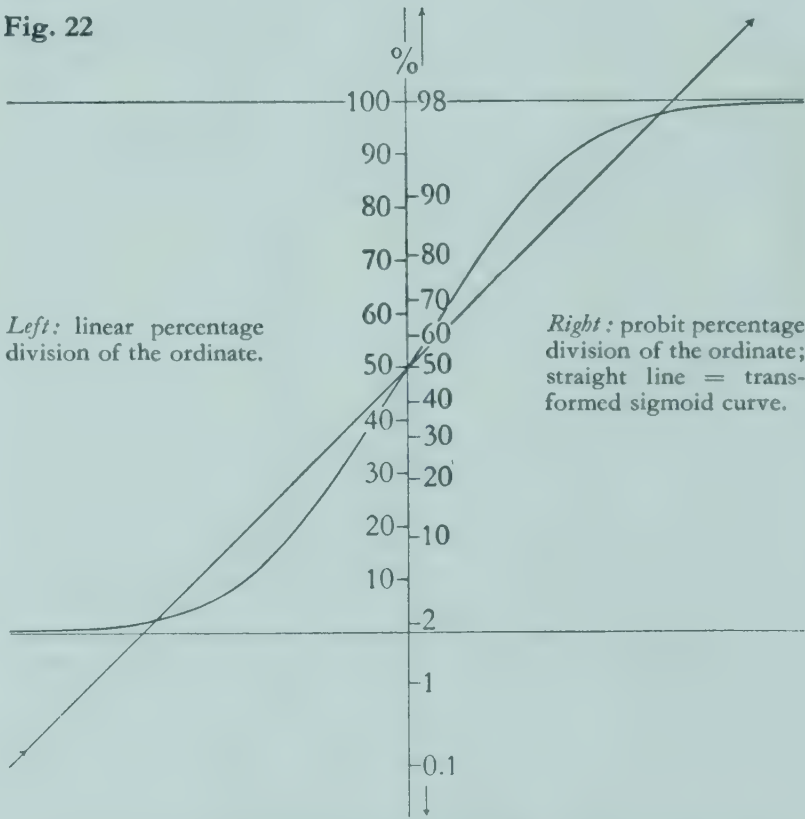
Fig. 21



This sigmoid curve may be transformed into a straight line by means of the probit transformation, whereby the frequency percentages (= areas $\times 100$) are converted into corresponding deviations of the normal distribution increased by the addition of

the number 5 and known as probits (see fig. 22). The probits may be obtained without the need of calculation from the table on pages 26 and 27.

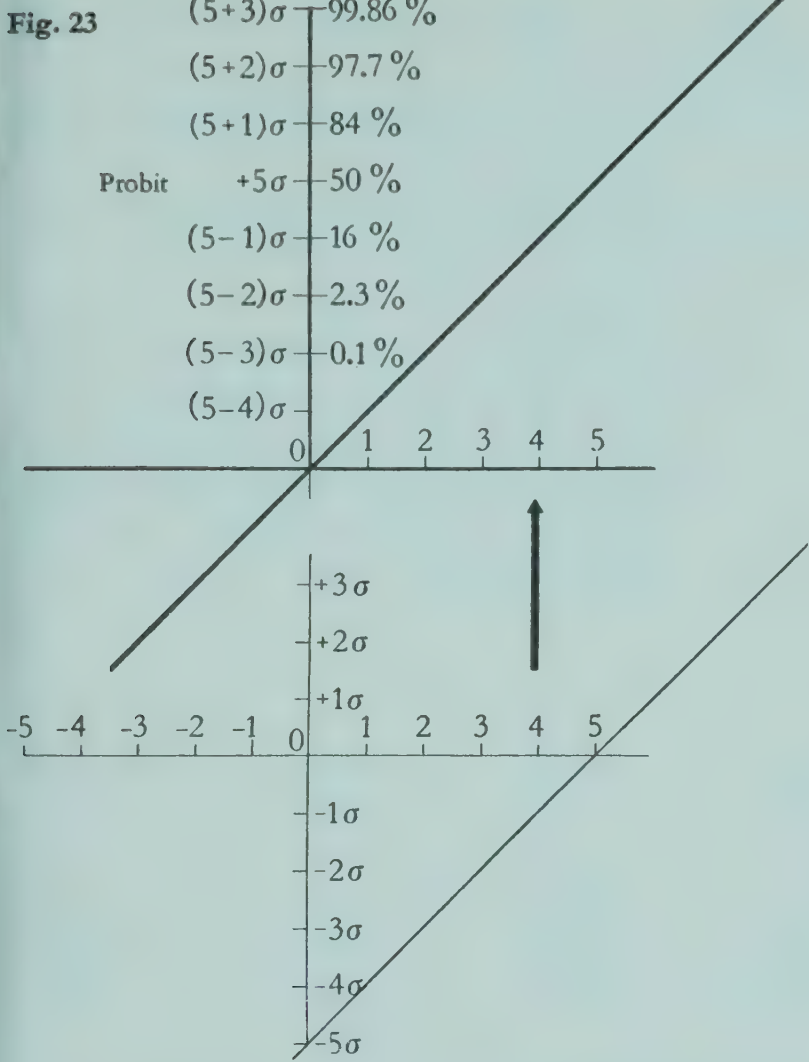
Fig. 22



In calculating the probits the deviations of the normal distribution are increased by 5 in order to bring the straight line out of the negative range (see fig. 23). Calculations are thus always made in the positive right upper quadrant of the co-ordinate system. In any case deviations greater than 5 (σ or $s > 5$) practically never occur.

If now x is a magnitude subject to chance variations a regression results as described in the previous section – the probit regression. To a large extent this may be evaluated by eye, but it also lends itself to extensive mathematical treatment. For a detailed description of this treatment the reader is referred to the literature*. Here a brief introduction only will be given, although this will suffice to yield quite accurate solutions. To begin with, some practical advice. In dosage investigations the doses should in-

* See page 48.



crease in geometrical progression and as a matter of routine the abscissa should carry the logarithmic values of these doses. In this way uniform intervals on the abscissa scale are obtained.

The numerical order of the doses 1, 2, 3, ... can therefore serve as the *x*-scale, with resultant simplification of the calculations. Conversion back to the absolute values is made at the end of the calculations.

The course of the calculations can best be demonstrated by means of an example.

Example 9. It is required to establish a 50% lethal dose (DL 50%). After a number of preliminary tests*, 7 concentrations of the substance, increasing in geometrical progression, are prepared and each tested on 6 experimental animals. The following result is obtained.

Solution (x)		Experimental animals			Empirical probit
		Total number	Died		
			Number	Per cent	
1	} n' = 7	6	0	0	—
2		6	1	16.6..	4.0
3		6	2	33.3..	4.6
4		6	4	66.6..	5.4
5		6	5	83.3..	6
6		6	5	83.3..	6
7		6	6	100	—

The **empirical probits** are obtained from the table on pages 26 and 27, entering with the percentages of animals which died. These empirical probits, rounded off to one decimal place, are now plotted as ordinates against the corresponding *x* numbers (solutions 1, 2, 3, ...) on millimeter graph paper. A regression line is now drawn through the middle (judging as well as possible by eye) of the resulting 5 points, or alternatively this is calculated by means of formulae (25) to (28) of the previous section. With experience this calculation can be made quickly enough, but it should be noted that with some practice regression lines can be drawn by eye with amply sufficient accuracy.

* The object of the preliminary tests is to decide on a suitable dosage progression.

		<i>x</i>	<i>y</i>	<i>x y</i>	<i>x</i> ²
Solution	2	2	4.0	8	4
»	3	3	4.6	13.8	9
»	4	4	5.4	21.6	16
»	5	5	6	30	25
»	6	6	6	36	36
Total (S)		20	26	109.4	90

$$\bar{x} = S(x) \div 5 = 4$$
$$\bar{y} = S(y) \div 5 = 5.2$$

$$b = \frac{S(xy) - \bar{x}S(y)}{S(x^2) - \bar{x}S(x)} = \frac{109.4 - 4 \times 26}{90 - 4 \times 20} = 0.54 \text{ (from 28)}$$

$$a = \bar{y} - b\bar{x} = 5.2 - 4 \times 0.54 = 3.04 \text{ (from 25)}$$

The **provisional regression line** is now drawn through the two points mean value (co-ordinates \bar{x}, \bar{y}) and *a* (co-ordinates *x* = 0, *y* = 3.04).

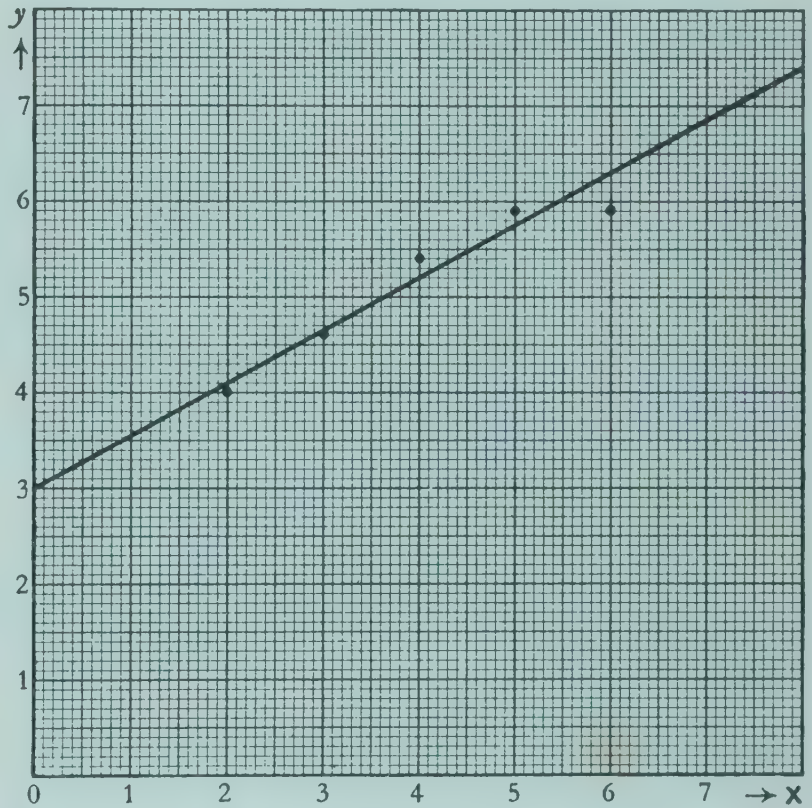


Fig. 24 Provisional regression line

The points of intersection of this line with *x* = 1, 2, 3, ... give the **provisional probits**.

<i>x</i>	Provisional probit
1	3.6
2	4.1
3	4.6
4	5.2
5	5.7
6	6.3
7	6.8

rounded off to one decimal place

From these provisional probits the **working probits**, with which the actual calculation is carried out, are now obtained as follows: in the case in which all the animals survived, the minimum working probit (table on page 28, column 2) corresponding to the provisional probit (column 1) is obtained. In the case in which all the animals died, the maximum working probit (column 4) corresponding to the provisional probit (column 1) is obtained.

Example: Solution 1, all animals survived, minimum working probit = working probit = 3.0606.
Solution 7, all animals died, maximum working probit = working probit = 7.2551.

In those cases where a proportion of the animals died, the ratio of the number of deaths to the number of animals treated is worked out for each solution (= percentage divided by 100). The range (column 3) corresponding to the provisional probit is then multiplied by this ratio, and the number so obtained added to the minimum working probit (column 2) in the same line of the table. The resulting sum represents the working probit for the particular solution.

Example: Solution 2, ratio of deaths to number of animals treated = 1:6 = 0.16.., range (corresponding prov. probit 4.1) = 3.7582, multiplied by 0.16.. = 0.62634. This number added to the corresponding min. working probit = 3.4083 + 0.62634 gives the working probit 4.03464.

The appropriate weighting coefficients must now be found. These coefficients (column 5) corresponding to the provisional probits

(column 1) are obtained and multiplied by the number of animals treated with each solution.

Example: Solution 1 (prov. probit = 3.6), weighting coefficient = 0.30199 × 6 = 1.81194.

This completes the basic numbers required for the further calculation. In the following text they will be given the names

Weighting coefficient = *w*
Working probit = *y*
Solution (concentration) = *x* = 1, 2, 3, ...

(The concentrations may not result in equidistant *x* values, but this is of no consequence. In this case working probits corresponding to equidistant *x* values are read off the provisional regression line, although these will not correspond to the actual concentrations of the test solutions.)

The present example gives then the figures

<i>y</i>	<i>w</i>	<i>w y</i>	<i>w y</i> ²	<i>w x y</i>	<i>w x</i>	<i>w x</i> ²
3.0606	1.81194	5.54562	16.97292	5.54562	1.81194	1.81194
4.03464	2.82864	11.41260	46.04549	22.82508	5.65728	11.31456
4.56942	3.60312	16.46417	75.23171	49.39251	10.80936	32.42808
5.42346	3.76452	20.41672	110.72926	81.66688	15.05808	60.23232
5.94115	3.18594	18.92815	112.45498	94.64075	15.92970	79.64850
5.89233	2.01534	11.87505	69.97171	71.25030	12.09204	72.55224
7.2551	1.07964	7.83290	56.82847	54.83030	7.55748	52.90236
Total (S)	18.28914	92.47515	488.23454	380.15144	68.91588	310.89000

The parameters of the **weighted** probit regression (from the weighted values *w x*, *w y*) are now

$$\bar{x} = S(w x) \div S(w) = 68.91588 \div 18.28914 = 3.768$$

(51)

$$\bar{y} = S(w y) \div S(w) = 92.47515 \div 18.28914 = 5.056$$

(52)

$$b = \frac{S(w x y) - \bar{x} S(w y)}{S(w x^2) - \bar{x} S(w x)} = \frac{380.15144 - 3.768131 \times 92.47515}{310.89000 - 3.768131 \times 68.91588} = \frac{\mathbf{A}}{\mathbf{B}} = \frac{31.69305}{51.20601} = 0.6189$$

(53)

The **abscissa of the 50 % lethal dose** is

$$\times DL\ 50\% = [(5 - \bar{y}) \div b] + \bar{x} = [-0.056287 \div 0.618932] + 3.7688 = 3.677$$

(54)

Before calculating the variance of the deviation $\times DL\ 50\%$, the values in the neighbourhood of this deviation must be tested for normal distribution (with χ^2).

$$\chi^2 DL\ 50\% = S(w y^2) - \bar{y} S(w y) - b \mathbf{A} = 488.23454 - 467.58118 - 19.61578 = 1.037; (\mathbf{A} \text{ from } 53)$$

(55)

The corresponding *P* lies between 98% and 95% (degree of freedom *n* = *n*' - 2 = 5), from which it may be assumed that the value is very probably normally distributed. In this case the variance can be calculated as follows:

$$\begin{aligned} \text{Variance } \times DL\ 50\% &= s^2 DL\ 50\% = \frac{1}{b^2} \left[\frac{1}{S(w)} + \frac{(\times DL\ 50\% - \bar{x})^2}{S(w x^2) - \bar{x} S(w x)} \right] = \frac{1}{b^2} \left[\frac{1}{S(w)} + \frac{(\times DL\ 50\% - \bar{x})^2}{\mathbf{B}} \right] \\ &= (0.0546772 - 0.0001615) \div b^2; (\mathbf{B} \text{ from } 53) \end{aligned}$$

(56)

$$\text{Standard deviation } s_{DL\ 50\%} = \sqrt{0.05452} \div b = 0.2335 \div 0.6189 = 0.377$$

It follows that $\times DL\ 50\% \pm 2 s = 3.677 \pm 0.754$, i.e. $\times DL\ 50\%$ lies between 2.92 and 4.43 in 95 cases out of 100*.

If χ^2 does not show a normal distribution (*P* $\bar{\leq}$ 0.05) then the limits of the *DL* 50% must be calculated as follows:

$$\pm \text{limits } DL\ 50\% = \bar{x} + \frac{1}{b \mathbf{A} - c^2} \left(\mathbf{A} (5 - \bar{y}) \pm c \sqrt{\mathbf{B} \left[\frac{b \mathbf{A} - c^2}{S(w)} + (5 - \bar{y})^2 \right]} \right); (\mathbf{A} \text{ and } \mathbf{B} \text{ from } 53)$$

(57)

where *c* = normal deviation of the desired safety threshold, e.g. 1.96 for *P* = 0.05.

In the example this would give limits *x* = 2.8 and 4.5.

* Since the doses have been plotted as logarithms, the limits of the actual doses do not lie symmetrically above and below the mean. These limits must therefore be determined with $\times DL\ 50\%$ and $s_{DL\ 50\%}$ as logarithms, and the logarithmic values obtained converted afterwards into actual concentrations.

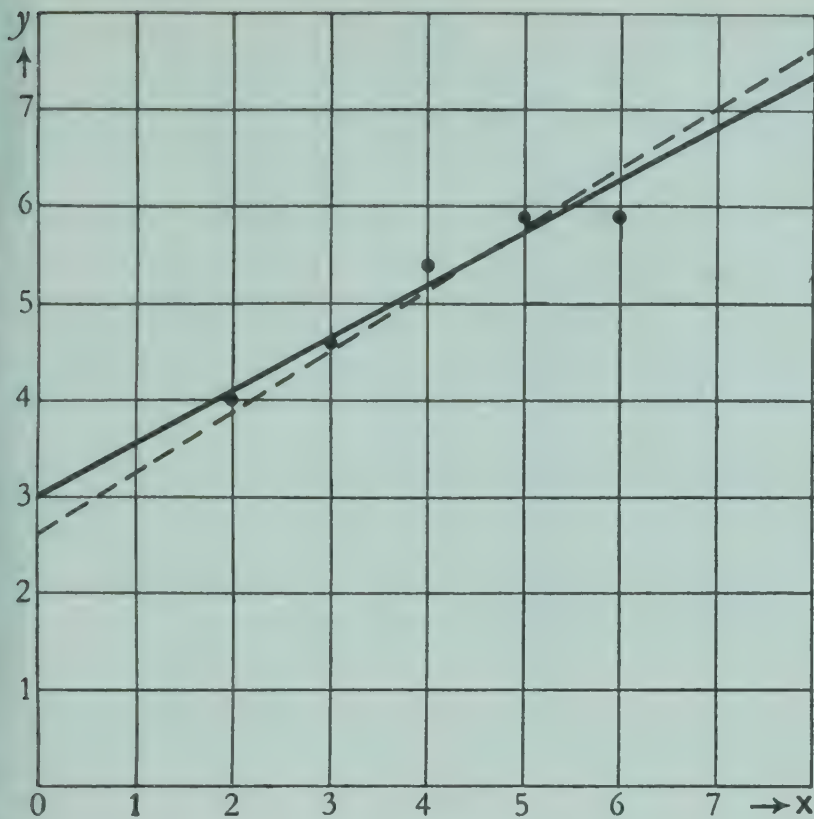


Fig. 25 Provisional } regression lines
Weighted }

When even greater accuracy is desired, a further doubly weighted regression line may be drawn with the aid of the weighted regression obtained as above, and the whole calculation repeated. As a rule, however, the single calculation is sufficient. If the experimental animals are subject to a natural mortality rate which can affect the experimental mortality, this factor must be taken into account in the calculation. The reader is here referred to the literature*.

Conclusion

We have seen that statistical methods provide us with a means of coping mathematically with the effects of chance. All these methods are based on the requirement that samples of a population, insofar as they are representative of that population, are a random selection from it. Only when this condition is fulfilled can the non-fortuitous nature of an event, whether it be an experimental result or any other kind of event, be demonstrated statistically with reasonable probability.

True random sampling is, however, very rare in medical practice. Hardly a single sample originating from a hospital or a doctor's practice can be considered as truly random, even when it appears to be so at first glance and all possible precautions have been taken. Such samples should be considered as definitely representative only of some more restricted population, and their interpretation limited accordingly. Particular caution is necessary with all pathological postmortem samples. It should not be overlooked that the cases of a dangerous illness which enter a hospital already represent a pre-selection. Death has kept the most severe cases at home.

Wherever there exists the least doubt regarding the real effect of a treatment, a drug, etc., tests involving untreated controls should be arranged. The controls must be subject to the same psychological conditions as the test subjects. In other words, they must believe themselves to be receiving exactly the same treatment as the test subjects, and likewise receive tablets, injections, etc., although of course of an inert nature. If, for example, it is desired to investigate the effect of the administration of oxygen to fatigued athletes, a control series of equally fatigued athletes should also receive "oxygen"—in this case ordinary air—under the same external conditions (apparatus, etc.). Only then can it be established whether the favourable effect is due to oxygen or simply to suggestion.

* See the following page.

Appendix

CHAUVENET's criterion

In a series of determinations it may happen that a few values differ markedly from the others. Such extreme values may chance to occur once in a hundred values, in other series twice in ten. In the latter case they have such a marked effect on the mean and variance that a strongly distorted picture of the behaviour of the population is presented. Such chance extremes can in general be eliminated by means of CHAUVENET's criterion. This lays down that, in relation to the number of measurements, all values greater than $\frac{1}{s} (x - \bar{x})$ can be eliminated. Here s is the standard deviation, $(x - \bar{x})$ the deviation from the mean, always taken as positive. For example, in a series of 30 measurements all values greater than $2.39 s$ (see the adjacent table) can be eliminated. After elimination of such values the mean and variance must of course be recalculated without regard to them. CHAUVENET's criterion could then eventually be again applied, and mean and variance again recalculated, etc. until no further values can be eliminated (cf. also the section on Mean and Variance, page 32 et seq.).

N	$\frac{1}{s} (x - \bar{x})$	N	$\frac{1}{s} (x - \bar{x})$
5	1.68	20	2.24
6	1.73	22	2.28
7	1.79	24	2.31
8	1.86	26	2.35
9	1.92	30	2.39
10	1.96	40	2.50
12	2.03	50	2.58
14	2.10	100	2.80
16	2.16	200	3.02
18	2.20	500	3.29

N = total range of the distribution; $(x - \bar{x})$ = deviation from the mean; s = standard deviation.

Calculation of mean and variance of samples subdivided into classes

Given is the distribution $f_1 x_1, f_2 x_2, f_3 x_3, \dots$, with the classes x_1, x_2, x_3, \dots and the occupation of the individual classes f_1, f_2, f_3, \dots . The class width k is $x_{(n+1)} - x_n$ and is the same for all classes. The total range N is $f_1 + f_2 + f_3 + \dots$. A provisional mean \bar{x}' is now formed, relative to one of the classes, and the deviations z of the classes from this mean worked out, expressed always in class units:

Example: With respect to the provisional mean, the first class has the deviation -1 , the second -2 , etc.

Then

Mean $\bar{x} = \bar{x}' + k \frac{S(fz)}{N}$ (58)

Variance $s^2 = k^2 \frac{1}{N-1} \left(S(fz^2) - \frac{[S(fz)]^2}{N} \right)$ (59)
(without SHEPPARD's correction)

$s = k \sqrt{\frac{1}{N-1} \left(S(fz^2) - \frac{[S(fz)]^2}{N} \right)}$ (60)
(without SHEPPARD's correction)

SHEPPARD's correction is based on the following circumstance:

In the subdivision of the individual values into classes a small error is made with regard to the chance selection of the values, resulting in a similar error in the calculated variance. This error may be corrected by subtraction of 0.0833 ($1/12$) from the variance calculated in class units (SHEPPARD's correction). This correction may be dispensed with in testing the significance of

differences, but it is otherwise recommended. Formulae (59) and (60) then become

$$s^2 = k^2 \left[\frac{1}{N-1} \left(S(fz^2) - \frac{[S(fz)]^2}{N} \right) - 0.0833 \right]$$

$$s = k \sqrt{\frac{1}{N-1} \left(S(fz^2) - \frac{[S(fz)]^2}{N} \right) - 0.0833}$$

(61) and (62)

Example 10. Erythrocyte diameters. Class width 0.4 μm.

Class	Frequency f	Deviation z	Frequency × Deviation fz	Frequency × square of deviation fz² = fz · z
5.6	5	−4	−20	80
6.0	78	−3	−234	702
6.4	144	−2	−288	576
6.8	479	−1	−479	479
7.2 = \bar{x}'	542	0	0	0
7.6	358	+1	+358	358
8.0	279	+2	+558	1116
8.4	99	+3	+297	891
8.8	15	+4	+60	240
9.2	1	+5	+5	25
	S(f) = N = 2000		S(fz) = 257	S(fz²) = 4467

$$\bar{x} = 7.2 + \left(0.4 \frac{257}{2000} \right) = 7.2514 \text{ }\mu\text{m}$$

(from 59 and 60): $s^2 = 0.4^2 \frac{4467 - 33.0}{1999} = 0.4^2 \cdot 2.218$; $s = 0.4 \sqrt{2.218} = 0.5958 \text{ }\mu\text{m}$ without SHEPPARD's correction

(from 61 and 62): $s^2 = 0.4^2 (2.218 - 0.0833) = 0.4^2 (2.135)$; $s = 0.4 \sqrt{2.135} = 0.5844 \text{ }\mu\text{m}$ with SHEPPARD's correction.

Bibliography: FINNEY, D. J., *Probit Analysis*, Cambridge University Press, 1952. FINNEY, D. J., *Statistical Method in Biological Assay*, CHARLES GRIFFINS & Co., London, 1952. FISHER, R. A., *The Design of Experiments*, OLIVER & BOYD, Edinburgh, 1953. FISHER, R. A., *Statistical Methods for Research Workers*, OLIVER & BOYD, Edinburgh, 1950. FISHER, R. A. and YATES, F., *Statistical Tables for Biological, Agricultural and Medical Research*, OLIVER & BOYD, Edinburgh, 1953. HILL, A. B., *Principles of Medical Statistics*, The Lancet Limited, London, 1950. HOSEMAN, H., *Die Grundlagen der statistischen Methoden für Mediziner und Biologen*, GEORG THIEME, Stuttgart, 1949. KENDALL, M. G., *The Advanced Theory of Statistics*, CHARLES GRIFFINS & Co., London, 1948. LINDER, A., *Planen und Auswerten von Versuchen*, BIRKHÄUSER, Basle, 1953. LINDER, A., *Statistische Methoden*, BIRKHÄUSER, Basle, 1951. MAINLAND, D., *The Treatment of Clinical and Laboratory Data*, OLIVER & BOYD, Edinburgh, 1938. WORTHING, A. G., and GEFFNER, J., *Treatment of Experimental Data*, John Wiley & Sons, Inc., New York, 1943.

Introduction

For the representation of physical phenomena we require, among other things, purely qualitative concepts, such as length, mass, time, acceleration, force, speed, etc.; these are designated kinds of values¹, or *qualities*² (as they will be referred to hereafter). Qualities are established and defined by suitable *methods* of measurement.

When a concrete determination is combined with the abstract quality, as for example in the concepts "velocity of light", "radius of the electron", etc., we then speak of *physical values*. A physical value may therefore be divided into two essential parts, one qualitative and the other quantitative. The measurement of a physical value thus requires not only the establishment of a *method* of measurement, but also the fixing of a *unit* of measurement, i.e. of a comparison value of the quality of a known and easily reproducible amount.

In physics qualities are related to each other both conceptually and formally by equations. Most qualities (and with them the physical values) may accordingly be reduced by substitution to a small number which cannot in the present state of science be related to each other physically. These qualities are known as the basic qualities, or *dimensions*, and must *a priori* be defined by basic rules of measurement. Purely numerical values, such as $\frac{1}{2}$, $\frac{1}{4}$, π , etc., or quotients of two like qualities, such as angles, specific gravity, etc., have no dimensions.

The number of dimensions necessary for the representation of any particular field of physics varies according to the nature of the field. Thus, two suffice for kinematics and three for mechanics, while the representation of thermodynamics, electrodynamics and photometry requires the introduction of a further dimension.

The nature of a system of measurement is determined unequivocally by the combination of fundamental dimensions on which it is based. Systems of measurement with differing dimensions are known as *unlike* systems, e.g. the Length-Mass-Time-systems (LMT-systems) in physics and the corresponding Length-Force-Time-systems (LFT-systems) in technology. The transition between two unlike systems may be effected by replacing the differing dimension (or basic quality) in the one system by the dimensional formula of the corresponding *derived quality* in the other system. Let us consider for example the transition from LFT to LMT dimensional formulae. While the dimensions L and T are the same in both, the dimension F (Force) of the LFT-systems has the dimensional formula LMT^{-2} in the LMT-systems. It follows that in the LFT dimensional formula expressing any quality we need only replace F by LMT^{-2} in order to arrive at the corresponding LMT dimensional formula.

Dimensions (or basic qualities) are assigned corresponding *basic units*. As the choice of the size of the basic units is merely a question of expediency, it follows that there exist the following parallel LMT-systems: the CGS-system (basic units: centimetre, gram, mean solar second), the MKS-system (basic units: metre, kilogram, mean solar second), the MTS-system (basic units: metre, metric ton, mean solar second), the FPS-system (basic units: foot, pound, second), etc. Systems such as these, with like dimensions but employing different basic units, are known as *like systems*.

In order to arrive at the units of derived qualities in any system of measurement, the dimensions in the appropriate dimensional formula are simply replaced by the corresponding basic units of the system. Thus, as already stated, the dimensional formula of force in the LMT-systems is LMT^{-2} . The unit of force in the CGS-system is therefore $cm\ g\ s^{-2}$, in the MKS-system $m\ kg\ s^{-2}$, in the MTS-system $m\ t\ sec^{-2}$, in the FPS-system $ft.\ lb.\ sec^{-2}$, etc. When such derived units are in frequent use they usually acquire special names, like the following units of force in the LMT-systems: $cm\ g\ s^{-2} = \text{dyne}$ (CGS-system), $m\ kg\ s^{-2} = \text{newton}$ (MKS-system), $m\ t\ sec^{-2} = \text{sthene}$ (MTS-system), $ft.\ lb.\ sec^{-2} = \text{poundal}$ (FPS-system).

Systems of measurement in which the derived units are equal to one are known as *standard* systems. Conversely, a derived unit of measurement equal to one is a unit standardized on the system in question.

The LMT-systems of measurement with decimal division of the units (time measurement excluded) are all based on the metric system and have long been internationally recognized in science and technology, although the FPS-system continues to be very largely used in technology in Great Britain, USA and other Anglo-Saxon countries. In other countries, the CGS-system, also known as the absolute system, and until now the most widely used in physics, is being displaced by the MKS-system, because the absolute electrical system of measurement (basic units: $m-s-V_{abs}-I_{abs}$) which has been internationally recognized since 1948, is standardized on the MKS-system. In Switzerland, for example, the latter has been the statutory system since 1950. It forms part of the GIORGI system, which conforms to the absolute electrical system of measurement except that it uses other dimensions. In France the MTS-system has been the statutory system since 1919. Also internationally recognized are the LFT-systems in technology, the cm-p-s-system (basic units: centimetre, pond, second, corresponding to the CGS-system) and the m-kp-s-system (basic units: metre, kilopond, second, corresponding to the MKS-system).

Method of writing the symbols for dimensions, units and constants

The following method is internationally recognized: Symbols for units are written in perpendicular script, symbols for qualities and physical quantities in *italics*. Small letters are used for the symbols of units with the exception of units which are named in memory of famous scientists. Symbols of such units are written with capital letters. Exceptions are the curie (c), the röntgen (r), and the rutherford (rd).

The modern tendency is to write the dimensional symbols in light-face GROTESQUE CAPITALS in place of the small italics used previously.

Metric convention

The decisions of the Metric Convention, to which 33 countries now subscribe, are to be found in the *Procès-Verbaux des Séances, Comité International des Poids et Mesures* and in the *Comptes-rendus de la Conférence Générale des Poids et Mesures*.

¹) FLEISCHMANN, R., *Z. Phys.*, **129**, 377, 1951.

²) HÄBERLI, F., *Schweiz. Arch. angew. Wiss. Techn.* **13**, 65, 113, 136, 1947.

Symbol or abbreviation	Name	Page	Symbol or abbreviation	Name	Page	Symbol or abbreviation	Name	Page
'	sexagesimal minute	57	G	giga-	7	μc	microcurie	70
"	sexagesimal second	57	G	gauss	67	μg (γ)	microgram (gamma)	55
°	degree	56, 57	Gal	galileo	59	μl	microlitre	53
A			Gb	gilbert	67	μm (μ)	micrometre (micron)	52
a	arc	53	H	hecto-	7	μmol	micromole	75
a	year (astronom.)	56	h	mean solar hour	56	μμ	micro-micron	52
ac. (A.)	acre	53	h	PLANCK's constant	62	N		
asb	apostilb	72	h	hectare	53	n	nano-	7
at	technical atmosphere	60	ha	hectolitre	54	n. mi.	nautical mile, sea mile	52
atm	physical atmosphere	61	hl	hectometre	52	nx	nox	72
Λ	ampere	65, 67	hm	horse-power	62	N	newton	59, 69
Λ. (ac.)	acre	53	h. p. (HP)	horse-power	62	N	normal solution	76
Å	angstrom	52	II	henry	69	O		
A. U.	astronomical unit	52	HP (h. p.)	horse-power	62	oz. ap. (℥ ap.)	ounce (apothecary)	55
B			HP. hr.	horse-power hour	61	oz. av. (℥ av.)	ounce (avoirdupois)	55
b (bar)	bar	60	Hz	Hertz (cycle per second)	59, 73	oz. fl. (℥ fl.)	ounce (fluid)	54
bbl.	barrel	54	I	inch	52	oz. t. (℥ t.)	ounce (troy)	55
bu.	bushel	54	in.	millicurie of intensity	71	Oe	oersted	67
BTU _{mean}	British Thermal Unit _{mean}	61	Imc	millicurie of intensity per hour (SIEVERT dose)	71	Ω	ohm	66
C			Imch			P		
c	centi-	7	J	joule	61	p	pico-	7
c	curie	70	K	kilo-	7	p	pond	59
c	carat	55	k	kilocycle	59	pc	parsec	52
c	centesimal minute	57	kc (kHz)	kilogram	55	ph	phot	72
c.	cycle	59	kg	kilopond	59	phon	phon	73
ca.	centare	53	kg* (kp)	kilogram atom	75	pk.	peck	54
cal	calorie	61	kg. atom	kilogram equivalent	75	pt.	pint	54
cc	centesimal second	57	kg. equiv	kilopond	59	pt.	point	52
ccm (cc, cm ³)	cubic centimetre	53	kgp (kp)	kilocycle	59	pz.	pièze	60
cd	candela (candle)	72	kHz (kc)	kilometre	52	P	poise	63
cg	centigram	55	km	kilomole	75	PS	horse-power (internat.)	62
cl	centilitre	53	kmol	kilopond	59	PSH	horse-power hour (internat.)	61
cm	centimetre	52	kp	kilogram equivalent	75	Q		
cps	cycle per second	59	kval	kilowatt	62	q.	quintal	56
cu. ft. (ft. ³)	cubic foot	54	kW	kilowatt hour	61	qt.	quart	54
cu. in. (in. ³)	cubic inch	54	kWh	dose constant	71	R		
cu. yd. (yd. ³)	cubic yard	54	K	degree Kelvin	56	r	röntgen	70
cwt. l.	hundredweight (long)	56	°K			rad	radian	57
cwt. sh.	hundredweight (short)	56	L	litre	53	rad	unit of corpuscular radiation	71
C	coulomb	66	l	pound (avoirdupois)	56	r. b. c.	relative biological effect	71
°C	degree (Centigrade, Celsius)	56	lb.	pound (apothecary)	55	rev	revolution	59
Cl	clausius	62	lb. ap.	pound (troy)	55	rd.	rod	52
CV	horse-power (internat.)	62	lb. t.	pound weight	60	reg. tn.	register ton	54
CVh	horse-power hour (internat.)	61	lb. wt. (Lb.)	lumen	72	rem	röntgen-equivalent-man	71
D			lm	lumen hour	72	rep	röntgen-equivalent physical	71
d	deci-	7	lmh	lumen second	72	°R	degree Réaumur	57
d	mean solar day	56	lms	lux	72	°Rank.	degree Rankine	56
d*	sidereal day	56	lx	lux second	72	Ry	rydberg	61
da	deca-	7	lxs	light year	52	S		
db	decibel	73	ly.	lambert	72	s	mean solar second	56
dg	decigram	55	La	pound weight	60	s*	sidereal second	56
dk	deca-	7	M	milli-	7	s. ap. (℥ ap.)	scruple (apothecary)	55
dkm	decametre	52	m	minute	56	sb	stilb	72
dl	decilitre	53	m	metre	52	sec	mean solar second	56
dm	decimetre	52	m ³	cubic metre (stere)	54	sk	skot	72
dr. ap. (℥ ap.)	drachm, dram (apothec.)	55	mb	millibar	60	sn	sthene	59
dr. av. (℥ av.)	dram (avoirdupois)	55	mc	millicurie	70	sq. ft. (ft. ²)	square foot	53
dr. fl. (℥ fl.)	drachm, dram (fluid)	54	mg	milligram	55	sq. in. (in. ²)	square inch	53
dr. t. (℥ t.)	drachm, dram (troy)	55	mg. equiv	milligram equivalent	75	sq. mi. (mi. ²)	square mile (statutory)	53
dwt.	pennyweight	55	mGal	milligal	59	sq. rd. (rd. ²)	square rod	53
dyn	dyne	59, 69	mi.	statutory mile, land mile	52	sq. yd. (yd. ²)	square yard	53
E			min	mean solar minute	56	S	siemens	67
emu	electromagnetic unit	64-69	min. (M)	minim	54	S. E. D.	skin erythema dose	70
equ. (equiv)	gram equivalent	75	mkp	metre kilopond	62	St	stokes	63
erg	erg	61, 69	ml	millilitre	53	T		
esu	electrostatic unit	64-69	mm	millimetre	52	t	ton (metric)	55
eV	electron-volt	61	mmol	millimole	75	tn. l.	ton (long)	56
F			mm H ₂ O	millimetre of water	61	tn. sh.	ton (short)	56
ft.	foot	52	mm Hg (Torr)	millimetre of mercury	61	T	tera-	7
ft. Lb.	foot-pound _{wt}	61	mμ (nm)	millimicron (nanometre)	52	Torr	Torricelli (mm Hg)	61
F	farad	66	mol	mole	75	TMU	thousandth mass unit	61
°F	degree Fahrenheit	56	M	mega-	7	V		
G			MU	unit of mass (nuclear physics)	55	val	gram equivalent	75
g	gram	55	μ	micro-	7	vol%	volume per cent	76
g	grade	57	μ (μm)	micron (micrometre)	52	V	volt	64
γ (μg)	gamma (microgram)	55	μb	microbar	60, 73	W		
gal.	gallon	54				w	watt	67
g. atom	gram atom	75				Wb	weber	69
g. equiv	gram equivalent	75				X		
gi.	gill	54				X. U.	X- or SIEGBAHN unit	52
gr.	grain	55				Y		
gr. wt.	grain weight	60				y	year	56
						yd.	yard	52

(Where there is a difference between British and US units, the equivalents of the latter, in other US units or metric units, are printed in *italics*)

Lengths					Metric equivalents
Inches (in.)	Feet (ft.)	Yards (yd.)	Rods (rd.)	Miles (mi.)	
1	0.083333 (¹ / ₁₂)	0.027778 (¹ / ₃₆)	0.00505051 (¹ / ₁₉₈)	0.0000157828	2.54000 (<i>2.54001</i>) centimetre
12	1	0.333333 (¹ / ₃)	0.0606061	0.000189394	0.304800 (<i>0.304801</i>) metre
36	3	1	0.181818	0.000568182	0.914399 (<i>0.914402</i>) metre
198	16.5	5.5	1	0.003125	5.02919 (<i>5.02921</i>) metres
63360	5280	1760	320	1	1.60934 (<i>1.60935</i>) kilometres

Area						Metric equivalents
Square inches (sq. in.)	Square feet (sq. ft.)	Square yards (sq. yd.)	Square rods (sq. rd.)	Acres (A.)	Square miles (sq. mi.)	
1	0.0069444 (¹ / ₁₄₄)	0.0007716 (¹ / ₁₂₉₆)	6.45159 (<i>6.45163</i>) sq. centim
144	1	0.1111 (¹ / ₉)	0.0036731	2.29568 × 10 ⁻⁵	3.58701 × 10 ⁻⁸	0.092903 sq. metre
1296	9	1	0.03305785	2.06612 × 10 ⁻⁴	3.22831 × 10 ⁻⁷	0.836126 (<i>0.836131</i>) sq. metre
39204	272.25	30.25	1	0.00625 (¹ / ₁₆₀)	9.765625 × 10 ⁻⁶	25.29276 (<i>25.29295</i>) sq. metres
6272640	43560	4840	160	1	0.0015625	40.46842 (<i>40.46873</i>) sq. decam
4.0154 × 10 ⁹	27878400	3097600	102400	640	1	2.589979 (<i>2.589998</i>) sq. kilom

Volume			Metric equivalents
Cubic inches (cu.in.)	Cubic feet (cu. ft.)	Cubic yards (cu. yd.)	
1	0.000578704 (¹ / ₁₇₂₈)	2.143347 × 10 ⁻⁵	16.3870 (<i>16.3872</i>) cu. centin
1728	1	0.0370370 (¹ / ₂₇)	0.0283167 (<i>0.0283170</i>) cu. metre
46656	27	1	0.764551 (<i>0.764559</i>) cu. metre

Capacity – Liquid Measure					Metric equivalents
Gills (gi.)	Pints (pt.)	Quarts (qt.)	Gallons (gal.)	Cubic inches (cu. in.)	
1	0.25 (¹ / ₄)	0.125 (¹ / ₈)	0.03125 (¹ / ₃₂)	8.6690 (<i>7.21875</i>)	142.06 (<i>118.29</i>) millilitres
4	1	0.5 (¹ / ₂)	0.125 (¹ / ₈)	34.677 (<i>28.875</i>)	0.56825 (<i>0.47317</i>) litre
8	2	1	0.25 (¹ / ₄)	69.355 (<i>57.749</i>)	1.13650 (<i>0.94633</i>) litre
32	8	4	1	277.27 (<i>231.00</i>)	4.54596 (<i>3.78533</i>) litres

Apothecaries' Fluid Measure				Metric equivalents
Minims min. or ℥	Fluid drachms (US: Fluid drams) fl. dr. or ℥ fl.	Fluid ounces fl. oz. or ℥ fl.	Pints (pt.)	
1	0.016667 (¹ / ₆₀)	0.0020833 (¹ / ₄₈₀)	0.00010417 (<i>0.00013021</i>)	0.05919 (<i>0.06161</i>) millilitre
60	1	0.125 (¹ / ₈)	0.00625 (<i>0.0078125</i>)	3.5514 (<i>3.6966</i>) millilitres
480	8	1	0.05 (<i>0.0625</i>)	28.430 (<i>29.573</i>) millilitres
9600 (<i>7680</i>)	160 (<i>128</i>)	20 (<i>16</i>)	1	0.56825 (<i>0.47317</i>) litre

Dry Measure					Metric equivalents
Pints (pt.)*	Quarts (qt.)*	Pecks (pk.)	Bushels (bu.)	Cubic inches (cu. in.)	
1	0.5 (¹ / ₂)	0.0625 (¹ / ₁₆)	0.015625 (¹ / ₆₄)	33.6003	0.550599 litre
2	1	0.125 (¹ / ₈)	0.03125 (¹ / ₃₂)	67.2006	1.101198 litres
16	8	1	0.25 (¹ / ₄)	554.6 (<i>537.605</i>)	9.0919 (<i>8.8096</i>) litres
64	32	4	1	2219.3 (<i>2150.42</i>)	36.3677 (<i>35.2383</i>) litres

Mass – Avoirdupois / Commercial					Metric equivalents
Grains (gr.)	Drams (dr. av.)	Ounces (oz. av.)	Pounds (lb. av.)	Tons (short) (tn. sh.)*	
1	0.03657143	0.0022857	0.00014286 (¹ / ₇₀₀₀)	64.798918 milligrams
27.34375	1	0.0625 (¹ / ₁₆)	0.00390625 (¹ / ₂₅₆)	1.771845 grams
437.5	16	1	0.0625 (¹ / ₁₆)	0.00003125	28.349527 grams
7000	256	16	1	0.0005	453.5924 grams
....	512000	32000	2000	1	907.18486 kilograms

Mass – Troy Weight				Metric equivalents
Grains (gr.)	Pennyweights (dwt.)	Ounces (oz. t.)	Pounds (lb. t.)	
1	0.041667 (¹ / ₂₄)	0.0020833 (¹ / ₄₈₀)	0.0001736111 (¹ / ₅₇₆₀)	64.798918 milligrams
24	1	0.05 (¹ / ₂₀)	0.0041667 (¹ / ₂₄₀)	1.555174 grams
480	20	1	0.083333 (¹ / ₁₂)	31.103481 grams
5760	240	12	1	373.24177 grams

Mass – Apothecaries' Weight					Metric equivalents
Grains (gr.)	Scruples (℥ or s. ap.)	Drachms (US: Drams) (℥ or dr. ap.)	Ounces (℥ or oz. ap.)	Pounds (lb. ap.)	
1	0.05 (¹ / ₂₀)	0.016667 (¹ / ₆₀)	0.0020833 (¹ / ₄₈₀)	0.0001736111 (¹ / ₅₇₆₀)	64.798918 milligrams
20	1	0.333333 (¹ / ₃)	0.041667 (¹ / ₂₄)	0.0034722 (¹ / ₂₈₈)	1.2959784 grams
60	3	1	0.125 (¹ / ₈)	0.0104167 (¹ / ₉₆)	3.8879351 grams
480	24	8	1	0.083333 (¹ / ₁₂)	31.103481 grams
5760	288	96	12	1	373.24177 grams

Medical Prescription Notation					
1 drachm (dram)	.. ℥ i, or ℥ j.	1/2 grain	.. gr. ss.	1/2 ounce	.. ℥ ss.
1 1/2 drachms	.. ℥ iss.	1 »	.. gr. i, or gr. j.	1 »	.. ℥ i, or ℥ j.
2 »	.. ℥ ii, or ℥ ij.	1 1/2 grains	.. gr. iss.	1 1/2 ounces	.. ℥ iss.
3 »	.. ℥ iii, or ℥ iij.	2 »	.. gr. ii, or gr. ij.	1/2 pint	.. Oss.
3 1/2 »	.. ℥ iiiss.	2 1/2 »	.. gr. iiss.	1 »	.. Oi, or Oj.
1 gallon	.. Ci, or Cj.	4 »	.. gr. iv.	1/2 scruple	.. ℥ ss.
		8 »	.. gr. viii, or gr. viij.	1 »	.. ℥ i, or ℥ j.
				1 1/2 scruples	.. ℥ iss.
				2 »	.. ℥ ii, or ℥ ij.

* US unit only.

Length

Dimension in all systems of measurement = L
MKS and MTS basic unit: metre (m); CGS basic unit: centimetre (cm)

The primary standard of length is defined as being the distance at 0 °C between two lines on a platinum–iridium bar deposited at the International Bureau of Weights and Measures in Sèvres; this is the Prototype Metre of the International Metric Convention.

Name	Symbol or abbreviation	MKS-Equivalent m	CGS-Equivalent cm	Remarks and other Equivalents
X-ray spectroscopic unit				
X-unit (SIEGBAHN)	X.U.	1.00202×10^{-13}	1.00202×10^{-11}	The SIEGBAHN X-unit is defined by the relation: $d_{18^\circ\text{C}}(\text{CaCO}_3) \equiv 3029.45 \text{ X. U.}$ = lattice constant of calcite.
Metric units				
Micro-micrometre (micro-micron)	$\mu\mu\text{m}$ ($\mu\mu$)	10^{-12}	10^{-10}	0.01 \AA ; 10^{-9} mm .
Ångström	Å	10^{-10}	10^{-8}	The Ångström unit is defined by the relation: $\lambda_{\text{Cd}} \equiv 6438.4696 \text{ \AA}$ = wave length of the red cadmium line in dry air at 760 mm Hg and 15°C, containing 0.03 vol% CO_2 .
Nanometre (millimicron)	nm ($\text{m}\mu$)	10^{-9}	10^{-7}	10 \AA ; 10^{-6} mm .
Micrometre (micron)	μm (μ)	10^{-6}	10^{-4}	10^4 \AA ; 0,001 mm.
Millimetre	mm	10^{-3}	10^{-1}	10^7 \AA ; 1000 μ .
Centimetre	cm	10^{-2}	1	10^8 \AA ; $10^4 \mu$.
Decimetre	dm	10^{-1}	10	10^9 \AA ; $10^5 \mu$.
Metre	m	1	10^2	10^{10} \AA ; $10^6 \mu$; 39.37 inches (Brit and US); 3.281 feet (Brit and US); 1.0936 yards (Brit and US); 6.2137×10^{-4} mile (statute); 5.3961×10^{-4} mile (nautical).
Decametre	dkm	10^1	10^3	
Hectometre	hm	10^2	10^4	
Kilometre	km	10^3	10^5	
Astronomical units				
Astronomical unit	A. U.	1.49504×10^{11}	1.49504×10^{13}	The A. U. is defined ¹ as the large semi-axis of the earth's orbit (a) and is derived from the large semi-axis of the earth a_\odot and the daily solar parallax π_\odot as $a \equiv a_\odot/\sin \pi_\odot$ $\cong a_\odot/\pi_\odot$.
Light year	ly.	9.4637×10^{15}	9.4637×10^{17}	The ly. is defined as the distance travelled by light in a vacuum during one astronomical year (see page 56).
Parsec	pc	3.08375×10^{16}	3.08375×10^{18}	The pc is defined as the distance of a fixed star of parallax $\pi = 1''$ from the sun = 3.2633 light years.
Siriometre		1.49504×10^{17}	1.49504×10^{19}	$\equiv 10^6 \text{ A. U.}$
Distance of Sirius		1.54187×10^{17}	1.54187×10^{19}	5 pc; 1,031,324 A. U.
British and US units				
Mil	(Brit) (US)	2.539998×10^{-5} 2.540005×10^{-5}	2.539998×10^{-3} 2.540005×10^{-3}	} 0.001 inch.
Inch	(Brit) (US)	{ } 2.539998×10^{-2} 2.540005×10^{-2}	{ } 2.539998 2.540005	
Foot	(Brit) (US)		} 12 inches; 1/3 yard.	
Yard	(Brit) (US)	{ } 9.143992×10^{-1} 9.144018×10^{-1}		{ } 9.143992×10 9.144018×10
Rod	(Brit) (US)		} 36 inches; 3 feet.	
Statute mile	(Brit) (US)	{ } 5.02919 5.029210		{ } 5.02919×10^2 5.029210×10^2
Nautical mile	(Brit) (US)		} 198 inches; 5.5 yards.	
	(Brit) (US)	{ } 1.609341×10^3 1.609347×10^3		{ } 1.609341×10^5 1.609347×10^5
	(Brit) (US)		} Land mile; 5280 feet; 1760 yards; 320 rods; 8 furlongs; 0.86836 mile (nautical); 1.69×10^{-13} light years.	
	(Brit) (US)	{ } 1.853181×10^3 1.85325×10^3		{ } 1.853181×10^5 1.85325×10^5
	(Brit) (US)		} Sea mile; the length of one minute of latitude of the meridian; 1.1516 statute miles.	
Typographical units				
Point	pt.	3.5278×10^{-4}	3.5278×10^{-2}	1/12 em; 1/72 inch (= 0.01389 inch); 0.035278 centimetre. 12 points; 1/6 inch.
Em, pica		4.2333×10^{-3}	4.2333×10^{-1}	

¹) Cf. WESTPHAL, W. H., *Physikalisches Wörterbuch*, Berlin, 1952.

Area

In all systems of measurement the unit derived from the dimensional formula = L²
MKS- and MTS-unit: square metre (m²); CGS-unit: square centimetre (cm²)

Name	Symbol or abbreviation	MKS-Equivalent m ²	CGS-Equivalent cm ²	Remarks and other Equivalents
Metric units				
Square micrometre (micron)	μ ²	10 ⁻¹²	10 ⁻⁸	
Square millimetre	mm ²	10 ⁻⁶	10 ⁻²	0.0015500 sq. inch.
Square centimetre	cm ²	10 ⁻⁴	1	0.15500 sq. inch; 0.0010764 sq. foot; 1.1960 × 10 ⁻⁴ sq. yard.
Square decimetre	dm ²	10 ⁻²	10 ²	15.500 sq. inches.
Square metre	m ²	1	10 ⁴	10 ⁻⁶ square kilometre; 10 ⁻⁴ hectare; 10.764 sq. feet (Brit and US); 1.1959 sq. yards (Brit and US).
Are (square decametre)	a (dkm ²)	10 ²	10 ⁶	119.59 sq. yards (Brit and US).
Hectare (square hectometre)	ha (hm ²)	10 ⁴	10 ⁸	100 ares.
Square kilometre	km ²	10 ⁶	10 ¹⁰	0.386100 sq. mile (US).
British and US units				
Square mil (Brit and US)		6.4516 × 10 ⁻¹⁰	6.4516 × 10 ⁻⁶	10 ⁻⁶ sq. inch (Brit and US).
Square inch (Brit)	{ sq. in. or in. ²	6.451589 × 10 ⁻⁴	6.451589	{ 0.000772 sq. yard; 1/144 or 0.00694 sq. foot.
(US)		6.451626 × 10 ⁻⁴	6.451626	
Square foot (Brit)	{ sq. ft. or ft. ²	9.29029 × 10 ⁻²	9.29029 × 10 ²	{ 144 sq. inches; 1/9 sq. yard.
(US)		9.29034 × 10 ⁻²	9.29034 × 10 ²	
Square yard (Brit)	{ sq. yd. or yd. ²	8.36126 × 10 ⁻¹	8.36126 × 10 ³	{ 1296 sq. inches; 9 sq. feet; 3.22831 × 10 ⁻⁷ sq. mile.
(US)		8.36131 × 10 ⁻¹	8.36131 × 10 ³	
Centare (metric)	ca.	1	10 ⁴	
Square rod (US)	{ sq. rd. or rd. ²	2.5293 × 10	2.5293 × 10 ⁵	1/160 acre.
Acre (Brit)	{ A. (ac.)	4.046849 × 10 ³	4.046849 × 10 ⁷	{ 4840 sq. yards.
(US)		4.046873 × 10 ³	4.046873 × 10 ⁷	
Square mile (statute) (Brit)	{ sq. mi. or mi. ²	2.589979 × 10 ⁶	2.589979 × 10 ¹⁰	{ 3.0976 × 10 ⁶ sq. yards; 640 acres.
(US)		2.589998 × 10 ⁶	2.589998 × 10 ¹⁰	

Volume

In all systems of measurements the unit derived from the dimensional formula = L³
MKS- and MTS-unit; cubic metre (m³); CGS-unit: cubic centimetre (cm³)

Name	Symbol or abbreviation	MKS-Equivalent m ³	CGS-Equivalent cm ³	Remarks and other Equivalents
Metric units				
Cubic millimetre	mm ³ or cmm	10 ⁻⁹	10 ⁻³	0.01623 minim (US); 0.01689 minim (Brit).
Microlitre	μl	1.000027 × 10 ⁻⁹	1.000027 × 10 ⁻³	See remarks under Litre.
Cubic centimetre	cm ³ or ccm	10 ⁻⁶	1	16.894 minims (Brit); 16.231 minims (US); 0.28157 drachm (fluid, Brit); 0.27051 dram (fluid, US); 0.061023 cu. inch; 0.035195 ounce (fluid, Brit); 0.033814 ounce (fluid, US); 0.0021134 pint (liquid, US); 0.0018162 pint (dry, US); 0.0010567 quart (liquid, US); 9.0808 × 10 ⁻⁴ quart (dry, US); 8.7988 × 10 ⁻⁴ quart (liquid, Brit); 3.531477 × 10 ⁻⁶ cu. foot (Brit); 3.531445 × 10 ⁻⁵ cu. foot (US); 1.3079 × 10 ⁻⁶ cu. yard (Brit and US).
Millilitre	ml	1.000027 × 10 ⁻⁶	1.000027	See remarks under Litre. 0.2705179 dram (fluid, US).
Centilitre	cl	1.000027 × 10 ⁻⁵	1.000027 × 10	See remarks under Litre.
Decilitre	dl	1.000027 × 10 ⁻⁴	1.000027 × 10 ²	See remarks under Litre.
Cubic decimetre	dm ³	10 ⁻³	10 ³	
Litre	l	1.000027 × 10 ⁻³	1.000027 × 10 ³	The litre is defined as the volume of one kilogram of air-free water at its maximum density (760 mm Hg and 3.98 °C). The litre so defined is 1.000027 times as large as the cubic decimetre. The litre is an internationally accepted measure of volume. It should always be employed for the measurement of volumes not of simple geometric form. For this purpose an accurate determination is made of the mass of a standard liquid at a known temperature which occupies the volume to be measured. Water has been agreed upon as the standard liquid. 61.025 cu. inches; 35.196 ounces (fluid, Brit); 33.8147 ounces (fluid, US); 2.1134 pints (liquid, US); 1.7598 pints (Brit); 1.056710 quarts (liquid, US); 0.87990 quart (Brit); 0.035316 cu. foot; 0.26417762 gallon (US); 0.21998 gallon (Brit); 0.0013080 cu. yard.

Volume (continued)

Name	Symbol or abbreviation	MKS-Equivalent m ³	CGS-Equivalent cm ³	Remarks and other Equivalents	
Metric units					
Cubic metre (stere)	m ³	1	10 ⁶	See remarks under Cubic centimetre (m ³ -equivalents = cm ³ -equivalents × 10 ⁶).	
Hectolitre	hl	1.000027	1.000027 × 10 ⁶	See remarks under Litre.	
British and US units					
Minim	(Brit) (US)	min. or m̄	$\left\{ \begin{array}{l} 5.9194 \times 10^{-8} \\ 6.161171 \times 10^{-8} \end{array} \right.$	$\left\{ \begin{array}{l} 5.9194 \times 10^{-2} \\ 6.161171 \times 10^{-2} \end{array} \right.$	0.061610 ml; 1/60 dram (fluid, US); 1/480 ounce (fluid, US); 1/61440 gallon (US).
Drachm (fluid)	(Brit)	dr.fl. or $\frac{1}{3}$ fl.	3.5515 × 10 ⁻⁶	3.5515	60 minims (Brit); 1/8 ounce (Brit).
Dram (fluid)	(US)	dr.fl. or $\frac{1}{3}$ fl.	3.6967 × 10 ⁻⁶	3.6967	The US “dram” corresponds to the British “drachm”. 3.6966 ml; 60 minims; 0.225586 cu. inch; 1/8 ounce (fluid, US).
Cubic inch	(Brit) (US)	cu.in. or in. ³	$\left\{ \begin{array}{l} 1.638703 \times 10^{-5} \\ 1.638716 \times 10^{-5} \end{array} \right.$	$\left\{ \begin{array}{l} 1.638703 \times 10^0 \\ 1.638716 \times 10^0 \end{array} \right.$	Compare US-cu. inch (the first 3 decimal places are the same). 16.3868 ml; 4.4329 drams (fluid); 0.5541 ounce (fluid, US) 0.02976 pint (dry, US); 5.78704 × 10 ⁻⁴ cu. foot; 2.14334 × 10 ⁻⁵ cu. yard.
Ounce (fluid)	(Brit) (US)	oz.fl. or $\frac{1}{16}$ fl.	$\left\{ \begin{array}{l} 2.84130 \times 10^{-5} \\ 2.95737 \times 10^{-5} \end{array} \right.$	$\left\{ \begin{array}{l} 2.84130 \times 10^0 \\ 2.95737 \times 10^0 \end{array} \right.$	480 minims; 8 drachms. 29.5729 ml; 480 minims; 8 drams (fluid); 1.80469 cu. inches 1/16 pint (liquid); 1/128 gallon.
Gill	(US) (Brit)	gi.	$\left\{ \begin{array}{l} 1.18295 \times 10^{-4} \\ 1.42065 \times 10^{-4} \end{array} \right.$	$\left\{ \begin{array}{l} 1.18295 \times 10^2 \\ 1.42065 \times 10^2 \end{array} \right.$	0.118292 litre; 1920 minims; 32 drams (fluid); 4 ounces (fluid); 1/4 pint (liquid); 1/8 quart (liquid); 1/32 gallon. 0.14206 litre; 1/4 pint (liquid); 5 ounces (fluid); 1/32 gallon.
Pint (liquid)	(US)	pt.	4.73179 × 10 ⁻⁴	4.73179 × 10 ²	0.473167 litre; 7680 minims; 128 drams (fluid); 28.875 cu. inches; 16 ounces (fluid); 4 gills; 0.83268 pint (Brit); 0.5 quart; 1/8 gallon; 0.016711 cu. foot; 6.1881 × 10 ⁻⁴ cu. yard.
(dry)	(US)		5.5061 × 10 ⁻⁴	5.5061 × 10 ²	0.550599 litre; 33.600 cu. inches; 1/64 bushel.
(liquid)	(Brit)		5.6826 × 10 ⁻⁴	5.6826 × 10 ²	0.56825 litre; 1/8 gallon; 0.5 quart; 1.20094 pints (liquid, US); 4 gills; 20 ounces (fluid).
Quart (liquid)	(US)	qt.	9.46358 × 10 ⁻⁴	9.46358 × 10 ²	0.946333 litre; 256 drams (fluid); 32 ounces (fluid); 8 gills; 2 pints (liquid); 1/4 gallon.
(dry)	(US)		1.10123 × 10 ⁻³	1.10123 × 10 ³	1.10120 litres; 2 pints (dry); 1/32 bushel.
(liquid)	(Brit)		1.136521 × 10 ⁻³	1.136521 × 10 ³	1.13650 litres; 2 pints (liquid); 1/4 gallon.
Gallon	(US) (Brit or Imperial)	gal.	$\left\{ \begin{array}{l} 3.785434 \times 10^{-3} \\ 4.546085 \times 10^{-3} \end{array} \right.$	$\left\{ \begin{array}{l} 3.785434 \times 10^3 \\ 4.546085 \times 10^3 \end{array} \right.$	3.7853 litres; 231.00 cu. inches; 128 ounces (fluid); 32 gills; 8 pints (liquid); 4 quarts (liquid); 0.83268 gallon (Brit) 0.13368 cu. foot; 0.004951 cu. yard. 4.54596 litres; 160 ounces (fluid); 32 gills; 8 pints (liquid); 4 quarts (liquid); 1.20094 gallons (US); 0.16054 cu. foot 1/8 bushel (dry).
Peck	(US) (Brit)	pk.	$\left\{ \begin{array}{l} 8.80981 \times 10^{-3} \\ 9.0922 \times 10^{-3} \end{array} \right.$	$\left\{ \begin{array}{l} 8.80981 \times 10^3 \\ 9.0922 \times 10^3 \end{array} \right.$	8.80958 litres; 16 pints; 8 quarts; 1/4 bushel. 9.0919 litres; 2 gallons.
Cubic foot	(Brit) (US)	cu.ft. or ft. ³	$\left\{ \begin{array}{l} 2.831677 \times 10^{-2} \\ 2.831702 \times 10^{-2} \end{array} \right.$	$\left\{ \begin{array}{l} 2.831677 \times 10^4 \\ 2.831702 \times 10^4 \end{array} \right.$	For equivalents see under Cubic foot (US). 1728 cu. inches; 59.844 pints (liquid, US); 29.922 quarts (liquid, US); 25.714 quarts (dry, US); 7.481 gallons (US) 6.229 gallons (Brit); 0.80357 bushel (US); 0.77861 bushel (Brit); 1/27 cu. yard; 0.01 register ton (Brit).
Bushel (dry)	(US)	bu.	3.523927 × 10 ⁻²	3.523927 × 10 ⁴	35.238 litres; 64 pints (dry); 32 quarts (dry); 1.2444 cu. feet 0.96895 bushel (Brit); 0.304785 barrel.
(dry)	(Brit)		3.636868 × 10 ⁻²	3.636868 × 10 ⁴	36.3677 litres; 8 gallons; 1.2843 cu. feet.
Barrel (dry) (liquid) (dry)	(US) (US) (Brit)	bbl.	$\left\{ \begin{array}{l} 1.15628 \times 10^{-1} \\ 1.1924 \times 10^{-1} \\ 1.63659 \times 10^{-1} \end{array} \right.$	$\left\{ \begin{array}{l} 1.15628 \times 10^5 \\ 1.1924 \times 10^5 \\ 1.63659 \times 10^5 \end{array} \right.$	3.281 bushels. 31.5 gallons. 36 gallons.
Cubic yard	(Brit) (US)	cu.yd. or yd. ³	$\left\{ \begin{array}{l} 7.64553 \times 10^{-1} \\ 7.64559 \times 10^{-1} \end{array} \right.$	$\left\{ \begin{array}{l} 7.64553 \times 10^5 \\ 7.64559 \times 10^5 \end{array} \right.$	See cu. yard (US). 764.54 litres; 4.6656 × 10 ⁴ cu. inches; 1616 pints (liquid, US); 202.0 gallons (US); 168.17 gallons (Brit); 27 cu. feet.
Shipping Ton	(US)		1.132681	1.132681 × 10 ⁶	
Register Ton	(Brit) (US)	reg.tn.	$\left\{ \begin{array}{l} 2.831670 \\ 2.831702 \end{array} \right.$	$\left\{ \begin{array}{l} 2.831670 \times 10^6 \\ 2.831702 \times 10^6 \end{array} \right.$	100 cu. feet.

Mass

Dimension in the LMT-systems = M
Basic unit in the corresponding systems of measurement: MKS-system: kilogram (kg)
CGS-system: gram (g)
MTS-system: ton (t)

Dimensional formula in the LFT-systems = L⁻¹F T² (see page 49)
Derived unit in the corresponding m-kp-s-system of technology: m⁻¹ kp s² = 9.80665 kg, for which the name hyl has been suggested. With the steadily increasing use of the MKS-system, this unit will cease to be significant. It has been seldom used up to now and has been generally replaced in technology by the ratio weight/acceleration due to gravity. In this case the technical unit = kp/9.80665 m s⁻² = kg of the MKS-system.
The primary standard of mass is defined by the Prototype Kilogram of the International Metric Convention deposited in the International Bureau of Weights and Measures in Sèvres.

Name	Symbol or abbreviation	MKS-Equivalent kg	CGS-Equivalent g	Remarks and other Equivalents
Unit of Mass (nuclear physics)	MU	1.6597 ₁ × 10 ⁻²⁷	1.6597 ₁ × 10 ⁻²⁴	The MU is defined as the mass of a hypothetical atom with a molecular weight ≡ 1 in the physical scale of atomic weights. Its mass, expressed in grams, is derived by use of AVOGADRO's number <i>A</i> (with respect to the physical scale of atomic weights): 1 MU ≡ 1/ <i>A</i> Ph.Sc.g. It is related to the Dalton by the relation 1 MU = 1/ <i>k_A</i> Dalton whereby <i>k_A</i> is the conversion factor 1.000279, between the physical and the chemical scales of atomic weights (SMYTHE-Factor).
Unit of Mass (atomic physics)	Dalton	1.6601 ₈ × 10 ⁻²⁷	1.6601 ₈ × 10 ⁻²⁴	The Dalton is defined as the mass of a hypothetical atom with a molecular weight of 1 in the chemical scale of atomic weights. Calculation analogous to that of the MU.
Metric units				
Microgram (gamma)	μg (γ)	10 ⁻⁹	10 ⁻⁶	
Milligram	mg	10 ⁻⁶	10 ⁻³	0.01543236 grain; 7.71618 × 10 ⁻⁴ scruple; 6.43015 × 10 ⁻⁴ pennyweight; 5.6438 × 10 ⁻⁴ dram (avoirdupois); 2.57206 × 10 ⁻⁴ dram (apothecary or troy); 3.52739 × 10 ⁻⁶ ounce (avoirdupois); 3.215074 × 10 ⁻⁵ ounce (apothecary or troy); 2.67923 × 10 ⁻⁶ pound (apothecary or troy); 2.2046 × 10 ⁻⁶ pound (avoirdupois).
Centigram	cg	10 ⁻⁵	10 ⁻²	0.1543236 grain.
Decigram	dg	10 ⁻⁴	10 ⁻¹	1.543236 grains.
Carat	c	2 × 10 ⁻⁴	2 × 10 ⁻¹	3.08647 grains.
Gram	g	10 ⁻³	1	For equivalents see under Milligram (× 10 ³).
Kilogram	kg	1	10 ³	35.273957 ounces (avoirdupois); 32.150742 ounces (apothecary or troy); 2.6792285 pounds (apothecary or troy); 2.2046223 pounds (avoirdupois); 0,022046223 hundredweight (short); 0.019684 hundredweight (long); 0.0011023112 ton (short); 9.842064 × 10 ⁻⁴ ton (long).
Metric Ton	t	10 ³	10 ⁶	For equivalents see under Kilogram (× 10 ³).
British and US units				
Grain	gr.	6.4798918 × 10 ⁻⁵	6.4798918 × 10 ⁻²	The unit grain is the same in the avoirdupois, apothecary, and troy systems (avoirdupois units for general use, apothecary = apothecary's weights, troy = weights for precious stones and precious metals). 64.798918 mg; 0.05000 scruple (apothecary); 0.0416667 pennyweight; 0.03657143 dram (avoirdupois); 0.016667 dram (apothecary); 0.0022857 ounce (avoirdupois); 0.0020833 ounce (apothecary or troy); 1/5760 or 1.736111 × 10 ⁻⁴ pound (apothecary or troy); 1/7000 or 1.42857 × 10 ⁻⁴ pound (avoirdupois).
Carat	c.	2 × 10 ⁻⁴	2 × 10 ⁻¹	
Scruple (apothecary)	s. ap. or ℥ ap.	1.2959784 × 10 ⁻³	1.2959784	20 grains; 0.7314286 dram (avoirdupois); 1/3 dram (apothecary or troy); 0.0457143 ounce (avoirdupois); 0.041667 ounce (apothecary or troy); 0.00347222 pound (apothecary or troy); 0.00285714 pound (avoirdupois).
Pennyweight	dwt.	1.55517 × 10 ⁻³	1.55517	24 grains; 1/20 ounce (apothecary or troy).
Dram (avoirdupois)	dr. av. or ʒ av.	1.771845 × 10 ⁻³	1.771845	27.34375 grains; 1.3671875 scruples; 0.4557292 dram (apothecary or troy); 1/256 or 0.00390625 pound (avoirdupois).
Drachm (Brit) } (apothecary Dram (US) } or troy)	dr. ap. or dr. t. or ʒ ap. or ʒ t.	3.8879351 × 10 ⁻³	3.8879351	60 grains; 3 scruples; 2.194286 drams (avoirdupois); 1/8 or 0.125 ounce (apothecary or troy); 1/96 or 0.01041667 pound (apothecary or troy).
Ounce (avoirdupois)	oz. av. or ʒ av.	2.8349527 × 10 ⁻²	2.8349527 × 10	437.5 grains; 16 drams (avoirdupois); 1/16 or 0.0625 pound (avoirdupois).
Ounce (apothecary or troy)	oz. ap. or oz. t. or ʒ ap. or ʒ t.	3.1103481 × 10 ⁻²	3.1103481 × 10	480 grains; 24 scruples; 20 pennyweights; 8 drams (apothecary or troy); 0.08333 pound (apothecary or troy).
Pound (apothecary or troy)	lb. ap. or lb. t.	3.732418 × 10 ⁻¹	3.732418 × 10 ²	5760 grains; 288 scruples; 240 pennyweights; 96 drams (apothecary or troy); 12 ounces (apothecary or troy), 0.822857 pound (avoirdupois).

Mass (continued)

Name	Symbol or abbreviation	MKS-Equivalent kg	CGS-Equivalent g	Remarks and other Equivalents
British and US units				
Pound (avoirdupois)	lb. av.	4.535924×10^{-1}	4.535924×10^2	7000 grains; 256 drams (avoirdupois); 16 ounces (avoirdupois); 1.2152778 pounds (apothecary or troy); 0.01 hundredweight (short); 0.0089286 hundredweight (long); 5×10^{-4} ton (short); 4.464286×10^{-4} ton (long).
Hundredweight (short)	cwt. sh.	4.535924×10^1	4.535924×10^4	1600 ounces (avoirdupois); 100 pounds (avoirdupois); 0.05 ton (short).
Hundredweight (long)	cwt. l.	5.080235×10^1	5.080235×10^4	112 pounds (avoirdupois); 0.05 ton (long).
Quintal (metric)	q.	10^2	10^5	
Ton (short, US)	tn. sh.	9.07185×10^2	9.07185×10^5	0.907185 metric ton; 2000 pounds (avoirdupois); 20 hundredweights (short); 0.89286 ton (long).
Ton (long, Brit and US)	tn. l.	1.016047×10^3	1.016047×10^6	1.016047 metric tons; 2240 pounds (avoirdupois); 22.4 hundredweights (short); 1.12000 tons (short).

Time

Dimension in all systems of measurement = T
Fundamental unit in all systems of measurement: second (s, sec, or ^s) = mean solar second.

The units for the measurement of time are derived from the earth’s rotation, which can only be defined and measured in relation to a point situated outside the earth. In everyday life the sun is used as the reference point, giving *solar time*, and in astronomy the system of the fixed stars, particularly the vernal point or vernal equinox, giving *sidereal time*.

The ellipticity of the earth’s orbit and the inclination of the ecliptic cause an irregular motion of the “true” sun, which is therefore unsuitable as a basis for uniform measurements of time. The true sun is therefore replaced by a “mean” sun, which by definition and as a basis for calculation is imagined to describe its apparent path in the celestial meridian with uniform speed in one year, and in such a way that its distance from the true sun remains a minimum and its passage through the vernal point coincides with that of a sun moving uniformly in the ecliptic.

The true solar day is defined as the difference in time between two consecutive passages of the true sun through the meridian of the observer, whilst the *mean solar day* (d) is determined by passages through the meridian of the mean sun. The difference between mean solar time and true solar time (or right ascension of the true sun minus right ascension of the mean sun) is known as the temporal equation and is to be found in all astronomical and nautical almanachs. The mean solar day is divided into 24 hours (h or ^h) of 60 minutes (min or ^m), each of which consists of 60 seconds (s, sec, or ^s). Thus is derived the second which is the basic time unit in all systems of measurement; it is the 86,400th part of the mean solar day.

The *sidereal day* (d*) is the period of time between two consecutive passages

of the vernal point at the meridian of the observer: 1 d* = 24 h* = 1440 min* = 86,400 s* = 86,164.09 mean solar seconds.

The year (a) as unit of time is defined as the time taken by the earth to describe its orbit around the sun. Three reference systems are in use in astronomy:

The *sidereal year* (a_{sid}) is related to the fixed stars and is given by the time required by the sun in its apparent celestial orbit to pass a given fixed star and to return to it (assuming that the fixed star has not altered its celestial position in the meantime).

The *tropical year* (a_{trop}) is given by the period of time between two passages of the vernal point by the true sun; the *astronomical year* (a_{astr}) or *annus fictus* is analogously defined by passages of the mean sun. The astronomical and tropical years differ only very slightly and can be regarded as equal.

The *anomalous year* (a_{anom}) is determined by the ellipticity of the earth’s orbit and is given by the period of time between two consecutive perihelial passages.

These various years are related to the mean solar day by the following equations:

1 a_{astr} = 365 d 5 h 48 min 46.0 s = 365.24220 d = 3.1556928 × 10⁷ s

1 a_{sid} = 365 d 6 h 9 min 9.5 s = 365.25636 d = 3.1558150 × 10⁷ s

1 a_{anom} = 365 d 6 h 13 min 53.0 s = 365.25964 d = 3.1558433 × 10⁷ s

Name	Symbol or abbreviation	Equivalents in all systems of measurement (mean solar time, statutory time)	
		seconds (s)	hours (h)
Sidereal second	s*	9.972696×10^{-1}	2.77019×10^{-4}
Mean solar second	s or sec	1	2.77777×10^{-4}
Mean solar minute	m or min	6×10	1.66666×10^{-2}
Mean solar hour	h	3.6×10^3	1
Sidereal day	d*	8.616409×10^4	2.3934×10
Mean solar day	d	8.640000×10^4	2.4000×10

Temperature

Dimension in all systems of measurement: degree or [°]
Basic unit in MKS-, CGS-, and MTS-systems: degree Centigrade ([°] C) or degree Kelvin ([°] K).
Basic unit in the Anglo-Saxon systems of measurement: degree Fahrenheit ([°] F) or degree Rankine ([°] Rank.)

The concepts *temperature* and *heat* (quantity of heat) are rigorously differentiated in physics. The same quantity of heat may be distributed over a larger or smaller quantity of the same substance, which has a lower temperature in the former case than in the latter. In this sense, it is also said that heat itself possesses a higher or lower temperature.

Heat is a form of energy (see Energy), whilst the temperature of a body is a measure of the average kinetic energy per degree of freedom of the constituent molecules. Since it is related to the average movement of the latter, the concept of temperature can only be applied to bodies consisting of a large number of molecules. This simple relationship no longer applies at very low temperatures.

In physics the scale of temperature is the thermodynamic or *absolute scale*. It is based on use of the 2nd Law of Thermodynamics and commences with the value 0 at absolute zero at which the volume and pressure of ideal gases disappear. The absolute temperature scale is subdivided in all systems of measurement with centesimal division into degrees Kelvin ([°] K), and in the Anglo-Saxon system into degrees Rankine ([°] Rank.). The degree Kelvin corresponds in magnitude to the degree Centigrade and the degree Rankine to the degree Fahrenheit. The zero of the absolute temperature scale corresponds to the absolute zero = 0° K = -273.16° C = 0° Rank. = -459.69° F.

The fixed points of the *Centigrade scale* are the freezing point of water (= 0° C)

Temperature (continued)

and the boiling point of water (= 100° C) at 760 mm of mercury; for the determination of the freezing point, water saturated with air must be used. The fundamental difference between the two fixed points thus amounts to 100 degrees.

The fixed points of the *Fahrenheit scale* (the statutory scale in Great Britain)

are also the freezing and boiling points of water but these are given the scale values of + 32 degrees and + 212 degrees, respectively, since Fahrenheit's original fixed points were given by a freezing mixture of ammonium chloride and ice (= 0° F) and the normal human body temperature (= 100° F). The fundamental difference in the Fahrenheit scale thus amounts to 180 degrees.

Name	Symbol or abbreviation	° Centigrade	Conversion into ° Fahrenheit
Degree Fahrenheit (conversion table degrees Fahrenheit/ Centigrade, see the next page)	° F	$x^{\circ}F = \frac{5}{9} (x - 32)^{\circ}C$	1
Degree Rankine	° Rank.	$x^{\circ}Rank. = \frac{5}{9} (x - 491.69)^{\circ}C$	$x^{\circ}Rank. = (x - 459.69)^{\circ}F$
Degree Centigrade (Celsius) (conversion table degrees Centigrade/ Fahrenheit, see the next page)	° C	1	$x^{\circ}C = \left(\frac{9}{5} x + 32\right)^{\circ}F$
Degree Kelvin	° K	$x^{\circ}K = (x - 273.16)^{\circ}C$	$x^{\circ}K = \left[\frac{9}{5} (x - 273.16) + 32\right]^{\circ}F$
Degree Réaumur	° R	$x^{\circ}R = \frac{5}{4} x^{\circ}C$	$x^{\circ}R = \left(\frac{9}{4} x + 32\right)^{\circ}F$

Angles

An angle, being the quotient of two dimensions, has no physical dimension (dimension = 1).

Name	Symbol or abbreviation	Equivalent in 400-grade division	Equivalent in 360-degree division
Centesimal second	cc	$10^{-4} g$	$9 \times 10^{-5} ^{\circ}$
Sexagesimal second	"	$3.08642 \times 10^{-4} g$	$2.77778 \times 10^{-4} ^{\circ}$
Centesimal minute	c	$10^{-2} g$	$9 \times 10^{-3} ^{\circ}$
Sexagesimal minute	'	$1.85185 \times 10^{-2} g$	$1.66667 \times 10^{-2} ^{\circ}$
Grade	g	1 g	$9 \times 10^{-1} ^{\circ}$
Degree	°	1.11111 g	1 °
Radian	rad	$6.366198 \times 10 g$	$5.729578 \times 10 ^{\circ}$

Velocity

Dimension in all systems of measurement = LT⁻¹

Derived unit in the MKS- and MTS-systems: metre per second (metre/second, m s⁻¹)

Derived unit in the CGS-system: centimetre per second (centimetre/second, cm s⁻¹)

Name	Symbol or abbreviation	MKS-Equivalent m s ⁻¹	CGS-Equivalent cm s ⁻¹	Remarks and other Equivalents
Metric units				
Centimetre/second	cm s ⁻¹	10^{-2}	1	0.03600 kilometre/hour; 0.600 metre/minute; 0.02237 mile (statute) per hour; 0.032808 foot per second.
Metre/minute	m min ⁻¹	1.6667×10^{-2}	1.6667	0.06 kilometre/hour; 3.281 feet per minute; 0.05468 foot per second; 0.03728 mile (statute) per hour.
Kilometre/hour	km h ⁻¹	2.77778×10^{-1}	2.77778×10	0.016667 kilometre/minute; 0.6214 mile (statute) per hour; 0.5396 knot (nautical mile per hour); 0.9113 foot per second.
Metre/second	m s ⁻¹	1	10^3	See centimetre/second ($\times 10^3$)
Kilometre/minute	km min ⁻¹	1.6667×10	1.6667×10^3	See metre/minute ($\times 10^3$)
British and US units				
Foot per minute	ft. min. ⁻¹	5.0801×10^{-3}	5.0801×10^{-1}	0.016667 foot per second; 0.011364 mile (statute) per hour.
Foot per second	ft. sec. ⁻¹	3.04803×10^{-1}	3.04803×10	1.09728 kilometres/hour; 0.6818 mile (statute) per hour; 0.5921 knot (nautical mile per hour).
Mile (statute) per hour	mi. hr. ⁻¹	4.47040×10^{-1}	4.47040×10	1.60934 kilometres/hour; 0.8684 knot (nautical mile per hour); 1.4667 feet per second.
Knot (nautical mile per hour)		5.148×10^{-1}	5.148×10	1.853 kilometres/hour; 1.1516 miles (statute) per hour; 1.689 feet per second.
Mile per minute	mi. min. ⁻¹	2.68224×10	2.68224×10^3	96.561 kilometres/hour; 52.104 knots; 88 feet per second.

Conversion of degrees Centigrade into degrees Fahrenheit and vice versa

— 50° C to 150° C ; — 58° F to 302° F
1 division corresponds to 1° C or 1° F

30° C to 45° C ; 86° F to 113° F
1 division corresponds to 1/10° C or 1/10° F



Angular velocity

Dimension in all systems of measurement = T⁻¹

Name	Symbol or abbreviation	Degrees/second °/s	Equivalents Revolutions/minute rev min ⁻¹	Radians/second rad s ⁻¹
Revolution/day (revolution ≡ 2π)	rev d ⁻¹	4.1666 × 10 ⁻³	6.944 × 10 ⁻⁴	7.27221 × 10 ⁻⁶
Degree/second	°/s	1	1.6667 × 10 ⁻¹	1.74533 × 10 ⁻²
Revolution/minute (revolution ≡ 2π)	rev min ⁻¹	6.0000	1	1.04719 × 10 ⁻¹
Radian/second	rad s ⁻¹	5.7296 × 10	9.5493	1
Revolution/second (revolution ≡ 2π)	rev s ⁻¹	3.6000 × 10 ²	6.0000 × 10	6.28319

Acceleration

Dimension in all systems of measurement = LT⁻²

Derived unit in the MKS- and MTS-systems: metre/second per second (m s⁻²)

Derived unit in the CGS-system: centimetre/second per second (cm s⁻²) = galileo (Gal)

Name	Symbol or abbreviation	MKS-Equivalent m s ⁻²	CGS-Equivalent cm s ⁻²	Other Equivalents
Metric units				
Milligal	mGal	10 ⁻⁶	10 ⁻³	
Galileo	Gal (cm s ⁻²)	10 ⁻²	1	0.03281 foot/second per second
Metre/second per second	m s ⁻²	1	10 ²	3.281 feet/second per second
British and US unit				
Foot/second per second	ft. sec. ⁻²	3.04801 × 10 ⁻¹	3.04801 × 10	

Angular acceleration

Name	Symbol or abbreviation	Revolutions/second per second rev s ⁻²	Equivalents Radians/second per second rad s ⁻²	Other Equivalents
Revolution/minute per minute	rev min ⁻²	2.7778 × 10 ⁻⁴	1.74533 × 10 ⁻³	0.01667 rev min ⁻¹ s ⁻¹
Degree/second per second	°/s ²	2.7778 × 10 ⁻³	1.74533 × 10 ⁻²	
Revolution/minute per second	rev min ⁻¹ s ⁻¹	1.6668 × 10 ⁻²	1.04719 × 10 ⁻¹	
Radian/second per second	rad s ⁻²	1.592 × 10 ⁻¹	1	9.549 rev min ⁻¹ s ⁻¹
Revolution/second per second	rev s ⁻²	1	6.28319	60 rev min ⁻¹ s ⁻¹ ; 3600 rev min ⁻²

Frequency

Dimension in all systems of measurement = T⁻¹

Basic unit in all systems of measurement: s⁻¹ = cycle/second (for vibrational frequency). The designation cycle/second is not permissible for the dimensionally similar frequency *f* of circular (angular) frequency $\omega = 2\pi f$.

The term cycle/second is known in the German-speaking countries as the Hertz (Hz). Kilocycle (kc) = kilohertz (kHz) = 1000 cycles/second.

Force, Weight

Dimensional formula in the LMT-systems = LMT⁻²

Derived units in the corresponding systems of measurement: MKS-system: newton (N) m kg s⁻²

CGS-system: dyne (dyn) cm g s⁻²

Dimension in the LFT-System = F

MTS-system: sthene (sn) m t s⁻²

Basic unit in the associated m-kp-s-system of technology: 9.80665 newtons = the weight of the mass of a kilogram at the standard acceleration of gravity $g_n = 9.80665 \text{ m s}^{-2}$. This unit is known as the kilopond (kp) in Germany, Austria, and Sweden. In France the designations Poinot or Fortin have been suggested. It is also abbreviated as kg* or kg_p. The general tendency is to use the newton as a unit of weight in technology also.

Name	Symbol or abbreviation	MKS-Equivalent N	CGS-Equivalent dyn	m-kp-s-Equivalent kp
Metric units				
Dyne	dyn	10 ⁻⁶	1	1.019716 × 10 ⁻⁶
Pond (gramweight)	p	9.80665 × 10 ⁻³	9.80665 × 10 ³	10 ⁻³
Newton	N	1	10 ⁶	1.019716 × 10 ⁻¹
Kilopond (kilogramweight)	kp	9.80665	9.80665 × 10 ⁶	1

Force, Weight (continued)

Name	Symbol or abbreviation	MKS-Equivalent N	CGS-Equivalent dyn	m-kp-s-Equivalent kp
British and US units				
Grain weight ¹	gr. wt.	6.3546×10^{-4}	6.3546×10	6.4799×10^{-5}
Poundal ²		1.38255×10^{-1}	1.38255×10^4	1.40981×10^{-2}
Pound weight ³	lb. wt. or Lb.	4.44822	4.44822×10^5	4.53592×10^{-1}

Density

Dimensional formula in the LMT-systems = L⁻³M

Derived units in the corresponding systems of measurement: MKS-system: kilogram per cubic metre (kg m⁻³)
CGS-system: gram per cubic centimetre (g cm⁻³)
MTS-system: metric ton per cubic metre (t m⁻³)

Dimensional formula in the LFT-systems = L⁻⁴FT²

In general the *density* of a body is the relation of its mass to its volume. The *specific gravity* of a body is the relation of its weight to the weight *at a definite temperature* (*) of an equal volume of water. It is, therefore, dimensionless being the relation between two like dimensions (see page 49). Practically speaking, the specific gravity of a substance is the same as the density. The specific gravities of gases are determined with respect to air at 760 mm Hg and 0 ° C instead of water. The specific gravity of air under these conditions, free of carbon dioxide and dry, is 0.001293, and with normal carbon dioxide content and 50% humidity, 0.07012919.

Name	Symbol or abbreviation	MKS-Equivalent kg m ⁻³	CGS-Equivalent g cm ⁻³	Other Equivalents
Metric units				
Gram/cubic metre	g m ⁻³	10 ⁻³	10 ⁻⁶	0.437 grain per cubic foot.
Kilogram/cubic metre	kg m ⁻³	1	10 ⁻³	0.06243 pound per cubic foot.
Gram/millilitre	g ml ⁻¹	9.99972×10^2	9.99972×10^{-1}	Numerically the same as the specific gravity of water at 3.98° C.
Gram/cubic centimetre	g cm ⁻³	10 ³	1	62.43 pounds per cubic foot.
Ton/cubic metre	t m ⁻³	10 ³	1	
British and US units				
Grain per cubic foot	gr. ft. ⁻³	2.288×10^{-3}	2.288×10^{-6}	
Demal (metric)		1	10 ⁻³	
Pound per cubic foot	lb. ft. ⁻³	1.6018×10	1.6018×10^{-2}	
Pound per gallon (Brit)	lb. gal. ⁻¹	9.9777×10	9.9777×10^{-2}	
Pound per gallon (US)	lb. gal. ⁻¹	1.1983×10^2	1.1983×10^{-1}	
Pound per cubic inch	lb. in. ⁻³	2.7680×10^4	2.7680×10	

Pressure

Dimensional formula in the LMT-systems = L⁻¹MT⁻²

Derived units in the corresponding systems of measurement:
MKS-system: newton per square metre (N m⁻²) ≡ m⁻¹ kg s⁻²
CGS-system: dyne per square centimetre (dyn cm⁻²) ≡ cm⁻¹ g s⁻² ≡ microbar (μb)
MTS-system: pièze (pz) ≡ m⁻¹ t s⁻²

Dimensional formula in the LFT-systems of technology = L⁻²F

Derived unit in the corresponding m-kp-s-system of technology: kilopond per square metre (kp m⁻²). The expression kp cm⁻² × 10⁴ is known as the technical atmosphere (at), and is the pressure unit mainly used in technology: 1 at = 9.80665 × 10⁴ N m⁻².

The expression dyn cm⁻² × 10⁶ is known as the bar (b or bar); the millibar (mb) is the present international unit of pressure in meteorology. The microbar (μb) is the unit for the pressure of sound.

Special units of pressure are the millimetre of water (mm H₂O) and the Torricelli (Torr), usually known as the millimetre of mercury (mm Hg). These designations should be avoided since they are dimensionally lengths. They are reserved for use as a measure of the height of the column of liquid exerting the given pressure. 760 mm Hg = one physical atmosphere (atm, formerly Atm).

Name	Symbol or abbreviation	MKS-Equivalents N m ⁻²	CGS-Equivalent (dyn cm ⁻²) μb	Other Equivalents			
				mm H ₂ O	mm Hg (Torr)	atm	at
Metric units							
Microbar (dyne per sq. centimetre)	μb (dyn cm ⁻²)	10 ⁻¹	1	1.01974×10 ⁻²	7.50062×10 ⁻⁴	9.86923×10 ⁻⁷	1.01972×10 ⁻⁶
Newton per square metre	N m ⁻²	1	10	1.01974×10 ⁻¹	7.50062×10 ⁻³	9.86923×10 ⁻⁶	1.01972×10 ⁻⁵
Kilopond per square metre (weight in kilos p.sq.metre)	kp m ⁻²	9.80665	9.80665×10	1.000028	7.35556×10 ⁻²	9.6784 ×10 ⁻⁵	10 ⁻⁴
Technical atmosphere (= 10 ⁴ kp m ⁻²)	at	9.80665×10 ⁴	9.80665×10 ⁵	1.000028×10 ⁴	7.35556×10 ³	9.6784 ×10 ⁻¹	1
Bar (= 10 ⁶ dyn cm ⁻²)	b or bar	10 ⁵	10 ⁶	1.01974×10 ⁴	7.50062×10 ³	9.86923×10 ⁻¹	1.01972

¹) 1 gr. wt. = 1 gr. × 32.1741 ft. sec.⁻² = 1 gr. × 9.80665 m s⁻².
²) 1 poundal = ft. × lb. av. × sec.⁻².
³) 1 lb. wt. (Lb.) = 1 lb. av. × 32, 1741 ft. sec.⁻² = 1 lb. av. × 9.80665 m s⁻².
(*) The temperatures are written as fractions, e.g. specific gravity of a substance at 20°/4°C means that the weight of the substance in question at 20° C was related to the weight of the same volume of water at 4° C. All specific gravities with respect to water at 4° C are numerically identical with the weight of a millilitre of the substance.

Pressure (continued)

Name	Symbol or abbrevi- ation	MKS- Equivalent N m ⁻²	CGS- Equivalent (dyn cm ⁻²) μb	Other Equivalents			
				mm H ₂ O	mm Hg	atm	at
Special pressure units							
Pressure of 1 mm column of water	mm H ₂ O mmHg or Torr	9.80638	9.80638×10	1	7.3554×10^{-2}	9.6781×10^{-5}	9.99972×10^{-5}
Pressure of 1 mm column of Hg, Torricelli		1.33322×10^3	1.33322×10^3	1.359548×10	1	1.3158×10^{-3}	1.35951×10^{-3}
Physical atmosphere (= 760 mm Hg)		atm	1.01325×10^5	1.01325×10^6	1.033257×10^4	7.6000×10^2	1
British and US units							
Pound _{wt} per square foot	Lb. ft. ⁻²	4.7880×10	4.7880×10^2	4.88256	3.5913×10^{-1}	4.7254×10^{-4}	4.8824×10^{-4}
Inch of water at 4° C		2.49082×10^3	2.49082×10^3	2.54000×10	1.86827	2.4583×10^{-3}	2.5399×10^{-3}
Foot of water at 4° C (39.1° F)		2.9889×10^3	2.9889×10^4	3.0479×10^2	2.241×10	2.9499×10^{-2}	3.0479×10^{-2}
Inch of mercury at 32° F		3.38639×10^3	3.38639×10^4	3.453×10^2	2.54000×10	3.3421×10^{-2}	3.4531×10^{-2}
Pound _{wt} per square inch		Lb. in. ⁻²	6.8947×10^3	6.8947×10^4	7.0309×10^2	5.1715×10	6.8046×10^{-2}

Energy (Work, Quantity of Heat)

Dimensional formula in the LMT-systems = L²MT⁻²

Derived units in the corresponding systems of measurement:

MKS-system: joule (J) = newton × metre = m²kg s⁻²

CGS-system: erg (erg) = dyne × centimetre = cm²g s⁻²

Dimensional formula in the LFT-systems = LF

Derived unit in the corresponding m-kp-s-system: metre-kilopond (mkp) = metre × kilopond = 9.80665 joules.

Since energy is stored or potential work it is measured in the same units as work. Fundamentally a body may possess energy in two ways, either as a result of its position with respect to other bodies in its vicinity (potential energy) or as a result of its motion (kinetic energy). In addition, each body possesses in the form of its mass *m* the potential energy *E* = *mc*₀² (*c*₀ = velocity of light in a vacuum). As a result the thousandth mass unit (TMU) is used in atomic physics as a unit of energy. Heat (quantity of heat) is the energy of molecular motion, and was formerly measured in calories, now in joules. The relation between these two units (1 cal₁₅ = 4.1854 joules) used to be known as the mechanical equivalent of heat, a constant now rendered obsolete by the present practice of measuring heat in joules.

Name	Symbol or abbrevi- ation	MKS-Equivalent J	CGS-Equivalent erg	Other Equivalents		
				eV	cal ₁₅	kWh
Unit in gaseous discharge physics and astrophysics						
Temperature degree ¹⁾	° K	$\triangle 1.380_4 \times 10^{-23}$	$\triangle 1.380_4 \times 10^{-16}$	$\triangle 8.617_8 \times 10^{-5}$	$\triangle 3.298_2 \times 10^{-24}$	$\triangle 3.834_5 \times 10^{-30}$
Units in atomic and nuclear physics						
Centimetre ^{-1 2)}	cm ⁻¹	$\triangle 1.985_5 \times 10^{-23}$	$\triangle 1.985_5 \times 10^{-16}$	$\triangle 1.239_5 \times 10^{-4}$	$\triangle 4.744 \times 10^{-24}$	5.515×10^{-30}
Electron-volt ³⁾	eV	$\triangle 1.6020 \times 10^{-19}$	$\triangle 1.6020 \times 10^{-12}$	1	$\triangle 3.827_5 \times 10^{-20}$	$\triangle 4.448_3 \times 10^{-26}$
Rydberg ⁴⁾	Ry	$2.177_6 \times 10^{-18}$	$2.177_6 \times 10^{-11}$	$\triangle 1.3594 \times 10$	5.203×10^{-19}	6.0465×10^{-25}
Thousandth mass unit ⁵⁾	TMU	$\triangle 1.491_6 \times 10^{-13}$	$\triangle 1.491_6 \times 10^{-6}$	$\triangle 9.312_1 \times 10^5$	$\triangle 3.563_9 \times 10^{-14}$	$\triangle 4.143_4 \times 10^{-20}$
Metric units						
Erg	erg	10^{-7}	1	$\triangle 6.242_1 \times 10^{11}$	2.3892×10^{-8}	2.77672×10^{-14}
Joule	J	1	10^7	$\triangle 6.242_1 \times 10^{18}$	2.3892×10^{-1}	2.77672×10^{-7}
Kilowatt hour	kWh	3.6000×10^6	3.6000×10^{13}	$\triangle 2.247_2 \times 10^{25}$	$8.601_1 \times 10^5$	1
Other international units						
15° Calorie ⁶⁾	cal ₁₅	4.1855	4.1855×10^7	$\triangle 2.612_7 \times 10^{19}$	1	1.1622×10^{-6}
Horse-power hour	CVh or PSh	2.647796×10^6	2.647796×10^{13}	$\triangle 1.652_8 \times 10^{25}$	$6.326_1 \times 10^5$	1
British and US units						
Foot-pound _{wt}	ft. Lb.	1.35582	1.35582×10^7	$\triangle 8.463_3 \times 10^{18}$	3.2393×10^{-1}	3.7647×10^{-7}
British Thermal Unit _{mean} ⁷⁾	BTU _{mean}	1.05579×10^3	1.05579×10^{10}	$\triangle 6.590_4 \times 10^{21}$	2.5225×10^2	2.9316×10^{-4}
Horse-power hour	HP. hr.	2.68452×10^6	2.68452×10^{13}	$\triangle 1.675_7 \times 10^{25}$	6.4139×10^5	7.4542×10^{-1}

¹⁾ 1° K is the kinetic energy of a molecule which possesses exactly the most probable velocity in the velocity distribution in an ideal gas at 1° K.

²⁾ 1 cm⁻¹ corresponds to the energy of a quantum of light of wave number γ = 1 cm⁻¹.

³⁾ 1 eV corresponds to the energy gained by an electron in an electric field in the form of kinetic energy after passage through a potential difference of 1 volt.

⁴⁾ 1 rydberg is the energy of ionization of the light hydrogen atom: 1 Ry = *hc*₀ × *R*_H.

⁵⁾ 1 TMU corresponds to the energy equivalent of the mass of a hypothetical molecule with the molecular weight on the physical scale (*M*)_{ph.sc.} = 10⁻³.

⁶⁾ 1 cal₁₅ = the quantity of heat required to raise 1 g of water from 14.5° C to 15.5° C = 10⁻³ frigorie = 10⁻⁶ thermie. The joule is used as unit of quantity of heat in accordance with international agreement. In comparative calorimetric determinations involving the heating of water, and wherever the use of the "calorie" is unavoidable, all data necessary for conversion to joules should be provided.

⁷⁾ 1 BTU_{mean} = $\left(\int_{32^{\circ}\text{F}}^{212^{\circ}\text{F}} c_{p_0}^{\delta}(\text{H}_2\text{O}) \times d\delta \right) / 180$; $\left(c_{p_0}^{\delta}(\text{H}_2\text{O}) \right) = \text{specific heat of water at normal physical pressure } p_0 \equiv 1 \text{ atm and at the temperature } \delta, \text{ with respect to one pound of water.}$

Power

Dimensional formula in the LMT-systems = L²MT⁻³

Derived units in the corresponding systems of measurement:

MKS-system: watt (W) ≡ 1 joule per second ≡ newton × metre per second ≡ m²kg s⁻³
CGS-system: erg/second (erg s⁻¹) ≡ dyne × centimetre per second ≡ cm²g s⁻³

Dimensional formula in the LFT-systems = LFT⁻¹

Derived unit in the corresponding m-kp-s-system of technology: metre-kilopond per second (mkp s⁻¹), which, multiplied by one hundred, is known as the poncelet in France. The units 75 mkp s⁻¹ (international horse-power) and 76.0402 mkp s⁻¹ (Brit and US horse-power) are still extensively used in technology.

Name	Symbol or abbreviation	MKS-Equivalent W	CGS-Equivalent erg s ⁻¹	Other Equivalents	
				mkp s ⁻¹	cal ₁₆ s ⁻¹
Metric units					
Ergs/second	erg s ⁻¹	10 ⁻⁷	1	1.019716 × 10 ⁻⁸	2.3892 × 10 ⁻⁸
Watt	W	1	10 ⁷	1.019716 × 10 ⁻¹	2.3892 × 10 ⁻¹
Metre-kilopond per second	mkp s ⁻¹	9.80665	9.80665 × 10 ⁷	1	2.3430
Poncelet		9.80665 × 10 ²	9.80665 × 10 ⁹	10 ²	2.3430 × 10 ²
Kilowatt	kW	10 ³	10 ¹⁰	1.019716 × 10 ²	2.3892 × 10 ²
Special power units					
15° Calorie per second	cal ₁₅ s ⁻¹	4.1855	4.1855 × 10 ⁷	4.2680 × 10 ⁻¹	1
Horse-power	CV or PS	7.35499 × 10 ²	7.35499 × 10 ⁹	7.50000 × 10	1.7573 × 10 ²
British and US units					
Foot-pound _{wt} per second	ft. Lb. sec. ⁻¹	1.35582	1.35582 × 10 ⁷	1.38255 × 10 ⁻¹	3.2393 × 10 ⁻¹
Horse-power	HP or h.p.	7.4570 × 10 ²	7.4570 × 10 ⁹	7.6040 × 10	1.7816 × 10 ²
British thermal unit _{mean} per second	BTU _{mean} per sec.	1.0557 ₉ × 10 ³	1.0557 ₉ × 10 ¹⁰	1.07661 × 10 ²	2.5225 × 10 ²

Action (Work as the Product Energy × Time)

Dimensional formula in the LMT-systems = L²MT⁻¹

Derived units in the corresponding systems of measurement:

MKS-system: joule × second (J s) ≡ newton × metre × second ≡ m²kg s⁻¹
CGS-system: erg × second (erg s) ≡ dyne × centimetre × second ≡ cm²g s⁻¹

Dimensional formula in the LFT-systems = LFT

Derived unit in the corresponding m-kp-s-system of technology: mkp s = 9.80665 J s.

Name	Symbol or abbreviation	MKS-Equivalent J s	CGS-Equivalent erg s	Other Equivalents	
				mkp s	PLANCK's constant
Units in quantum and atomic physics					
PLANCK's constant	<i>h</i>	6.625×10^{-34}	6.625×10^{-27}	$6.75_6 \times 10^{-34}$	1
Electron volt \times second	eV s	$\triangle 1.6020 \times 10^{-19}$	$\triangle 1.6020 \times 10^{-12}$	$\triangle 1.633_6 \times 10^{-20}$	$\triangle 2.418_1 \times 10^{14}$
Metric units					
Erg \times second ($\equiv 10^{-7}$ J s)	erg s	10^{-7}	1	1.0197×10^{-8}	$1.509_4 \times 10^{26}$
Joule \times second ($\equiv 10^7$ erg s)	J s	1	10^7	1.0197×10^{-1}	$1.509_4 \times 10^{23}$
Metre-kilopond \times second	mkp s	9.80665	9.80665×10^7	1	$1.480_2 \times 10^{24}$
Special unit					
15° Calorie \times second	cal ₁₅ s	4.1855	4.1855×10^7	4.2680×10^{-1}	6.318×10^{23}

Entropy

Dimensional formula in the LMT-systems = L²MT⁻² degree⁻¹

Derived units in the corresponding systems of measurement:

MKS-system: joule per degree Centigrade (J °C⁻¹) ≡ m²kg s⁻² °C⁻¹ ≡ 10⁻⁷ erg °C⁻¹
CGS-system: erg per degree Centigrade (erg °C⁻¹) ≡ cm²kg s⁻² °C⁻¹ ≡ 10⁻⁷ J °C⁻¹

Dimensional formula in the LFT-systems = LF degree⁻¹

Derived unit in the corresponding m-kp-s-system of technology:

metre-kilopond per degree Centigrade (mkp °C⁻¹) = 9.80665 J °C⁻¹

The special entropy unit clausius (Cl) = 15° calories per degree Centigrade (cal₁₅ °C⁻¹) has lost its significance since the recent introduction of the joule as the unit of quantity of heat in place of the calorie.

1 J °C⁻¹ ≡ 10⁷ erg °C⁻¹ = 0.2389 Cl; 1 Cl = 4.1854 J °C⁻¹ = 4.1854 × 10⁷ erg °C⁻¹

Dynamic Viscosity

Dimensional formula in the LMT-systems = $L^{-1}MT^{-1}$

Derived units in the corresponding systems of measurement:

MKS-system: newton \times second per square metre ($N\ s\ m^{-2}$) $\equiv m^{-1}\ kg\ s^{-1} \equiv 10\ poise$

CGS-system: poise (P) = dyne \times second per square centimetre ($dyne\ cm^{-2}$) $\equiv cm^{-1}\ g\ s^{-1} \equiv 0.1\ N\ s\ m^{-2}$

Foot-Pound-Second-system (avoirdupois): pound per foot per second ($lb.\ ft.^{-1}\ sec.^{-1}$) = poundal second per square foot
 $\equiv 1.48816\ N\ s\ m^{-2} \equiv 14.8816\ P$

Dimensional formula in the LFT-systems = $L^{-2}FT$

Derived units in the corresponding systems of measurement in technology:

m-kp-s-system: kilopond \times second per square metre ($kp\ s\ m^{-2}$) = $9.80665\ N\ s\ m^{-2}$

Foot-Pound-Second-system (avoirdupois): pound_{wt} second per square foot ($Lb.\ sec.\ ft.^{-2}$) = $47.8802\ N\ s\ m^{-2}$
 $\equiv 4.8824\ kp\ s\ m^{-2}$

Kinematic Viscosity

Dimensional formula in all systems of measurement = L^2T^{-1}

Derived units:

MKS-system: square metre per second ($m^2\ s^{-1}$) $\equiv 10^4\ stokes$
 square metre per hour ($m^2\ h^{-1}$) = $2.7778\ m^2\ s^{-1}$

CGS-system: stokes (St) = square centimetre per second ($cm^2\ s^{-1}$) $\equiv 10^{-4}\ m^2\ s^{-1}$

Foot-Pound-Second-system (avoirdupois): square foot per second ($ft.^2\ sec.^{-1}$) = $0.0092903\ m^2\ s^{-1}$
 square foot per hour ($ft.^2\ hr.^{-1}$) = $2.58064 \times 10^{-5}\ m^2\ s^{-1}$

Surface Tension

Dimensional formula in the LMT-systems = MT^{-2}

Derived units in the corresponding systems of measurement:

MKS-system: newton per metre ($N\ m^{-1}$) $\equiv kg\ s^{-2} \equiv 10^3\ dyn\ cm^{-1} = 1.0197 \times 10^{-1}\ kp\ m^{-1}$

CGS-system: dyne per centimetre ($dyn\ cm^{-1}$) $\equiv g\ s^{-2} \equiv 10^{-3}\ N\ m^{-1} = 1.0197 \times 10^{-4}\ kp\ m^{-1}$

Dimensional formula in the LFT-systems = $L^{-1}F$

Derived unit in the corresponding m-kp-s-system of technology:

kilopond per metre ($kp\ m^{-1}$) = $9.80665\ N\ m^{-1}$

Thermal Conductivity

Dimensional formula in the LMT-systems = $LMT^{-3}\ degree^{-1}$

Derived units in the corresponding systems of measurement:

MKS-system: joule per metre per second per degree Centigrade ($J\ m^{-1}\ s^{-1}\ ^\circ C^{-1}$) \equiv watt per metre per $^\circ C$ ($W\ m^{-1}\ ^\circ C^{-1}$)
 $\equiv m\ kg\ s^{-3}\ ^\circ C^{-1} \equiv 10^5\ erg\ cm^{-1}\ s^{-1}\ ^\circ C^{-1} = 2.3892_9 \times 10^{-3}\ cal_{15}\ cm^{-1}\ s^{-1}\ ^\circ C^{-1}$

CGS-system: erg per centimetre per second per degree Centigrade ($erg\ cm^{-1}\ s^{-1}\ ^\circ C^{-1}$) $\equiv cm\ g\ s^{-3}\ ^\circ C^{-1}$
 $\equiv 10^{-5}\ J\ m^{-1}\ s^{-1}\ ^\circ C^{-1} \equiv 10^{-5}\ m^{-2}\ ^\circ C^{-1} = 2.3892_9 \times 10^{-8}\ cal_{15}\ cm^{-1}\ s^{-1}\ ^\circ C^{-1}$

Special unit: 15° calorie per centimetre per second per degree Centigrade ($cal_{15}\ cm^{-1}\ s^{-1}\ ^\circ C^{-1}$)
 $\equiv 4.1854 \times 10^7\ erg\ cm^{-1}\ s^{-1}\ ^\circ C^{-1} = 4.1854 \times 10^3\ J\ m^{-1}\ s^{-1}\ ^\circ C^{-1} = 4.1854 \times 10^3\ W\ m^{-1}\ ^\circ C^{-1}$

Dimensional formula in the LFT-systems = $FT^{-1}\ degree^{-1}$

Coefficient of Heat Transfer

Dimensional formula in the LMT-systems = $MT^{-3}\ degree^{-1}$

Derived units in the corresponding systems of measurement:

MKS-system: watt per square metre per degree Centigrade ($W\ m^{-2}\ ^\circ C^{-1}$) $\equiv J\ m^{-2}\ s^{-1}\ ^\circ C^{-1} \equiv kg\ s^{-3}\ ^\circ C^{-1}$
 $\equiv 10^{-7}\ W\ cm^{-2}\ ^\circ C^{-1} \equiv 10^3\ erg\ s^{-1}\ cm^{-2}\ ^\circ C^{-1} = 2.3892_9 \times 10^{-5}\ cal_{15}\ cm^{-2}\ s^{-1}\ ^\circ C^{-1}$

CGS-system: erg/second per square centimetre per degree Centigrade ($erg\ s^{-1}\ cm^{-2}\ ^\circ C^{-1}$) $\equiv g\ s^{-3}\ ^\circ C^{-1}$
 $\equiv 10^{-3}\ W\ m^{-2}\ ^\circ C^{-1} \equiv 10^{-7}\ W\ cm^{-2}\ ^\circ C^{-1} = 2.3892_9 \times 10^{-8}\ cal_{15}\ cm^{-2}\ s^{-1}\ ^\circ C^{-1}$

Dimensional formula in the LFT-systems = $L^{-1}FT^{-1}\ degree^{-1}$

The systems of electrical measurement may be divided into two groups: systems based on a representation of electricity and magnetism which is defined by a three-dimensional theory of action at a distance, and systems based on a representation defined by four-dimensional field theory.

The definition of electrical qualities by a theory of action at a distance with the three dimensions LMT originates from the period when only the usual mechanical methods of measurement were available to the experimenter in electricity and magnetism. Definition by field theory came more and more into use with the development of specifically electrical methods of measurement and of the field theory of electrodynamics. It is characterized by being based on four fundamental measurements (and thus on four fundamental qualities, see page 49) of which at least one is specifically electrical, e.g. a measurement of resistance or of charge. The qualities defined by the field theory may accordingly be reduced to four basic qualities (dimensions) of which at least one is specifically electrical, e.g. to the dimensions LMT ϵ_0 (ϵ_0 = absolute permittivity) or LMT μ_0 (μ_0 = absolute permeability) or LMT ϵ_0 (ϵ_0 = absolute permittivity), etc. In practice, in conformity with OHM's Law, a combination of two electrical methods of measurement is usually used (potential combined with current or resistance) leading to the choice of two fundamental electrical units V and A for the *absolute electrical system of measurement* (dimensions LTUI = length, time, potential, current; basic units m-s-V-A = metre, second, volt, ampere). This system, internationally recognized since 1948, is based on the MKS Ω -system originally proposed by GIORGI, which in turn is based on the MKS-system. Its fourth dimension, the absolute ohm, is defined by fixing a numerical value for the absolute permeability μ_0 , measured in metres, seconds and ohms, so that

$$\mu_0 = 10^{-7} 4 \pi \Omega \text{ s m}^{-1}$$

The absolute ohm unit can thus be embodied in a resistance coil of suitable form and determined by an induction measurement. Conversion from the GIORGI m-kg-s- Ω -system to the absolute m-s-V-A-system is carried out by means of the following equations:

$$J \text{ (joule)} = \text{m}^2 \text{ kg s}^{-2}$$
$$V = \sqrt{\frac{J \Omega}{s}}$$

whence

$$V = \text{m kg}^{1/2} \text{ s}^{-3/2} \Omega^{1/2}$$

$$\Omega = \text{VA}^{-1}$$
$$A = \sqrt{\frac{J}{\Omega \text{ s}}}$$
$$A = \text{m kg}^{1/2} \text{ s}^{-3/2} \Omega^{-1/2}$$

The energy unit J (joule) and thus the units of force N (newton) and of power W (watt) of the absolute m-s-V-A-system are accordingly identical with the corresponding units of the MKS-system. The remaining units therefore also correspond and these two systems are steadily displacing other systems in science and technology.

Up to now, the systems of measurement defined by a theory of action at a distance with the three dimensions LMT and the basic units cm, g, s (the electromagnetic and electrostatic CGS-systems) have been much employed in physics on account of their correspondence with the CGS-system of mechanics. The units of these systems are obtained *formally* by setting the absolute permeability μ_0 or the absolute permittivity ϵ_0 equal to unity in the LMT μ_0 - or LMT ϵ_0 -systems, and representing the dimensions LMT by the corresponding units cm, g, s. The LMT μ_0 -system thus leads to the electromagnetic and the LMT ϵ_0 -system to the electrostatic CGS-system. Since $\epsilon_0 \mu_0 c^2 = 1$ (c_0 = velocity of light, abbreviated to c in the following), $\epsilon_0 = 1/c^2$ when $\mu_0 = 1$, and $\mu_0 = 1/c^2$ when $\epsilon_0 = 1$. The constant c_0 therefore appears as a factor in the interconversion of these systems.

The dimensions of the electrical systems of measurement described only partially correspond, i.e. the systems are unlike systems based on fundamentally different definitions (theory of action at a distance and field theory). The units of the various systems for one and the same quality, e.g. electrical field strength, cannot therefore be equated since although they are numerically equal they have different dimensions. This circumstance is not of practical importance since it is primarily the numerical values which are of interest when comparing measurements based on the various systems. It is accorded recognition in the following tables by the use of the symbol \triangle for numerically equal but dimensionally unequal equivalents. The units of the CGS electrical systems of measurement are given the following symbols: emu = electromagnetic CGS-unit, esu = electrostatic CGS-unit.

Electrical or Magnetic Quality (Symbol) Dimensional system System of measurement	Dimensions Unit	Symbol or abbreviation	Equivalents (\triangle indicates numerical but not dimensional equivalence c = velocity of light in a vacuum in centimetres per second = 2.9979×10^{10})
Electrical Potential (U) (Potential difference, electro-motive force) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	U volt $L^{3/2} M^{1/2} T^{-2} \mu_0^{1/2}$ $\text{cm}^{3/2} \text{g}^{1/2} \text{s}^{-2}$ $L^{1/2} M^{1/2} T^{-1} \epsilon_0^{-1/2}$ $\text{cm}^{1/2} \text{g}^{1/2} \text{s}^{-1}$	V emu esu	$\triangle 10^8 \text{ emu} \triangle 10^8/c \text{ esu} (= 3.3357 \times 10^{-8} \text{ esu})$ $\triangle 10^{-8} \text{ V} \triangle 1/c \text{ esu} (= 3.3357 \times 10^{-11} \text{ esu})$ $\triangle 10^{-8} c \text{ V} (= 2.9979 \times 10^8 \text{ V})$ $\triangle c \text{ emu} (= 2.9979 \times 10^{10} \text{ emu})$

Electrical or Magnetic Quality (Symbol) Dimensional system System of measurement	Dimensions Unit	Symbol or abbreviation	Equivalents (\triangle indicates numerical but not dimensional equivalence c = velocity of light in a vacuum in centimetres per second = 2.9979×10^{10})
Electric Current Strength (I) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	I ampere $L^{1/2} M^{1/2} T^{-1} \mu_0^{-1/2}$ $cm^{1/2} g^{1/2} s^{-1}$ $L^{3/2} M^{1/2} T^{-2} \epsilon_0^{1/2}$ $cm^{3/2} g^{1/2} s^{-2}$	A emu esu	$\triangle 10^{-1} \text{ emu} \triangle 10^{-1} c \text{ esu} (= 2.9979 \times 10^9 \text{ esu})$ $\triangle 10 \text{ A} \triangle c \text{ esu} (= 2.9979 \times 10^{10} \text{ esu})$ $\triangle 10/c \text{ A} (= 3.3357 \times 10^{-10} \text{ A}) \triangle 1/c \text{ emu}$ $(= 3.3357 \times 10^{-11} \text{ emu})$
Electric Current Density (S) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	$L^{-2} I$ ampere/square metre $L^{-3/2} M^{1/2} T^{-1} \mu_0^{1/2}$ $cm^{-3/2} g^{1/2} s^{-1}$ $L^{-1/2} M^{1/2} T^{-2} \epsilon_0^{1/2}$ $cm^{-1/2} g^{1/2} s^{-2}$	$A m^{-2}$ emu esu	$\triangle 10^{-5} \text{ emu} \triangle 10^{-5} c \text{ esu} (= 2.9979 \times 10^5 \text{ esu})$ $\triangle 10^5 \text{ A m}^{-2} \triangle c \text{ esu} (= 2.9979 \times 10^{10} \text{ esu})$ $\triangle 10^5/c \text{ A m}^{-2} (= 3.3357 \times 10^{-6} \text{ A m}^{-2}) \triangle 1/c \text{ emu}$ $(= 3.3357 \times 10^{-11} \text{ emu})$
Electrical Field Strength (E) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	$L^{-1} U$ volt/metre $L^{1/2} M^{1/2} T^{-2} \mu_0^{1/2}$ $cm^{1/2} g^{1/2} s^{-2}$ $L^{-1/2} M^{1/2} T^{-1} \epsilon_0^{-1/2}$ $cm^{-1/2} g^{1/2} s^{-1}$	$V m^{-1}$ emu esu	$\triangle 10^6 \text{ emu} \triangle 10^6/c \text{ esu} (= 3.3357 \times 10^{-8} \text{ esu})$ $\triangle 10^{-6} \text{ V m}^{-1} \triangle 1/c \text{ esu} (= 3.3357 \times 10^{-11} \text{ esu})$ $\triangle 10^{-6} c \text{ V m}^{-1} (= 2.9979 \times 10^4 \text{ V m}^{-1}) \triangle c \text{ emu}$ $(= 2.9979 \times 10^{10} \text{ emu})$
Electrical Displacement (D) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	$L^{-2} TI$ coulomb/square metre $L^{-3/2} M^{1/2} \mu_0^{-1/2}$ $cm^{-3/2} g^{1/2}$ $L^{-1/2} M^{1/2} T^{-1} \epsilon_0^{1/2}$ $cm^{-1/2} g^{1/2} s^{-1}$	$C m^{-2}$ emu esu	$\triangle 4\pi/10^5 \text{ emu} (= 1.25663 \times 10^{-4} \text{ emu})$ $\triangle 4\pi c/10^5 \text{ esu} (= 3.7671 \times 10^6 \text{ esu})$ $10^5/4\pi \text{ C m}^{-2} (= 7.9577 \times 10^3 \text{ C m}^{-2}) \triangle c \text{ esu}$ $(= 2.9979 \times 10^{10} \text{ esu})$ $10^5/4\pi c \text{ C m}^{-2} (= 2.6544 \times 10^{-7} \text{ C m}^{-2}) \triangle 1/c \text{ emu}$ $(= 3.3357 \times 10^{-11} \text{ emu})$
Absolute Permittivity (ϵ_0) (dielectric constant of a vacuum, electric space constant) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	$L^{-1} T U^{-1} I$ farad/metre $L^{-2} T^2 \mu_0^{-1}$ $cm^{-2} s^2$ ϵ_0 1	$F m^{-1}$ emu 1 [esu]	$\triangle 4\pi/10^{11} \text{ emu} (= 1.25663 \times 10^{-10} \text{ emu})$ $\triangle 4\pi c^2/10^{11} [\text{esu}] (= 3.7673 \times 10^6 [\text{esu}])$ $\triangle 10^{11}/4\pi \text{ F m}^{-1} (= 7.9577 \times 10^9 \text{ F m}^{-1}) \triangle c^2 [\text{esu}]$ $(= 8.9867 \times 10^{20} [\text{esu}])$ $\triangle 10^{11}/4\pi c^2 \text{ F m}^{-1} (= 8.854 \times 10^{-12} \text{ F m}^{-1})$ $\triangle 1/c^2 \text{ emu} (= 1.1127 \times 10^{-11} \text{ emu})$

Electrical or Magnetic Quality (Symbol) Dimensional system System of measurement	Dimensions Unit	Symbol or abbreviation	Equivalents (\triangle indicates numerical but not dimensional equivalence c = velocity of light in a vacuum in centimetres per second = 2.9979×10^{10})
Dielectric Polarization (P) Dimensional system LTUI Abs.el.syst.of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	$L^{-2} TI$ coulomb/square metre $L^{-3/2} M^{1/2} \mu_0^{-1/2}$ $cm^{-3/2} g^{1/2}$ $L^{-1/2} M^{1/2} T^{-1} \epsilon_0^{1/2}$ $cm^{-1/2} g^{1/2} s^{-1}$	$C m^{-2}$ emu esu	$\triangle 10^{-5} emu \triangle 10^{-5} c esu (= 2.9979 \times 10^5 esu)$ $\triangle 10^5 C m^{-2} \triangle c esu (= 2.9979 \times 10^{10} esu)$ $\triangle 10^5/c C m^{-2} (= 3.3357 \times 10^{-6} C m^{-2}) \triangle 1/c emu$ (= $3.3357 \times 10^{-11} emu$)
Electric Moment (M_e) Dimensional system LTUI Abs.el.syst.of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	$LT I$ coulomb \times metre $L^{3/2} M^{1/2} \mu_0^{-1/2}$ $cm^{3/2} g^{1/2}$ $L^{5/2} M^{1/2} T^{-1} \epsilon_0^{1/2}$ $cm^{5/2} g^{1/2} s^{-1}$	$C m$ emu esu	$\triangle 10 emu \triangle 10 c esu (= 2.9979 \times 10^{11} esu)$ $\triangle 10^{-1} C m \triangle c esu (= 2.9979 \times 10^{10} esu)$ $\triangle 10^{-1}/c C m (= 3.3357 \times 10^{-12} C m) \triangle 1/c emu$ (= $3.3357 \times 10^{-11} emu$)
Relative Electrical Susceptibility (K) Dimensional system LTUI Abs.el.syst.of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	1 1 1 1 1 1	 1 [Abs] 1 [emu] 1 [esu]	 $\triangle 1/4\pi [emu] (= 7.9577 \times 10^{-2} [emu]) \triangle 1/4\pi [esu]$ $\triangle 4\pi \times 10 [Abs] (= 1.2566 \times 10 [Abs]) \triangle 1 [esu]$ $\triangle 4\pi \times 10 [Abs] (= 1.2566 \times 10 [Abs]) \triangle 1 [emu]$
Electric Charge (Q) Dimensional system LTUI Abs.el.syst.of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	TI coulomb (= A s) $L^{1/2} M^{1/2} \mu_0^{-1/2}$ $cm^{1/2} g^{1/2}$ $L^{3/2} M^{1/2} T^{-1} \epsilon_0^{1/2}$ $cm^{3/2} g^{1/2} s^{-1}$	C emu esu	$\triangle 10^{-1} emu \triangle 10^{-1} c esu (= 2.9979 \times 10^9 esu)$ $\triangle 10 C \triangle c esu (= 2.9979 \times 10^{10} esu)$ $\triangle 10/c C (= 3.3357 \times 10^{-10} C) \triangle 1/c emu$ (= $3.3357 \times 10^{-11} emu$)
Electrical Capacity (C) Dimensional system LTUI Abs.el.syst.of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	$TU^{-1} I$ farad (= A s/V) $L^{-1} T^2 \mu_0^{-1}$ $cm^{-1} s^2$ $L \epsilon_0$ cm	F emu cm (esu)	$\triangle 10^{-9} emu \triangle 10^{-9} c^2 esu (= 8.9867 \times 10^{11} esu)$ $\triangle 10^9 F \triangle c^2 esu (= 8.9867 \times 10^{20} esu)$ $\triangle 10^9/c^2 F (= 1.1127 \times 10^{-12} F) \triangle 1/c^2 emu$ (= $1.1127 \times 10^{-21} emu$)
Electrical Resistance (R) Dimensional system LTUI Abs.el.syst.of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	UI^{-1} ohm (= VA $^{-1}$) (1 megohm = 10^6 ohms) $LT^{-1} \mu_0$ $cm s^{-1}$ $L^{-1} T \epsilon_0^{-1}$ $cm^{-1} s$	Ω emu esu	$\triangle 10^9 emu \triangle 10^9/c^2 esu (= 1.1127 \times 10^{-12} esu)$ $\triangle 10^{-9} \Omega \triangle 1/c^2 esu (= 1.1127 \times 10^{-21} esu)$ $\triangle 10^{-9} c^2 \Omega (= 8.9867 \times 10^{11} \Omega) \triangle c^2 emu$ (= $8.9867 \times 10^{20} emu$)

Electrical or Magnetic Quality (Symbol) Dimensional system System of measurement	Dimensions Unit	Symbol or abbreviation	Equivalents (\triangle indicates numerical but not dimensional equivalence c = velocity of light in a vacuum in centimetres per second = 2.9979×10^{10})
Electrical Conductivity (γ) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	$L^{-1} U^{-1} I$ siemens/metre (= $\Omega^{-1} m^{-1}$) $L^{-2} T \mu_0^{-1}$ $cm^{-2} s$ $T^{-1} \epsilon_0$ s^{-1}	$S m^{-1}$ ($\Omega^{-1} m^{-1}$) emu esu	$\triangle 10^{-11} emu \triangle 10^{-11} c^2 esu (= 8.9867 \times 10^9 esu)$ $\triangle 10^{11} S m^{-1} \triangle c^2 esu (= 8.9867 \times 10^{20} e\text{-}u)$ $\triangle 10^{11}/c^2 S m^{-1} (= 1.1127 \times 10^{-10} S m^{-1})$ $\triangle 1/c^2 emu (= 1.1127 \times 10^{-21} emu)$
Electric Power (P) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Dimensional system LMT ϵ_0 Electromagnetic CGS-system Electrostatic CGS-system	UI watt (= VA) $\left. \begin{array}{l} L^2 MT^{-3} \\ \text{erg/second} \\ (= cm^2 g s^{-3}) \end{array} \right\}$	W erg s ⁻¹	$\equiv 10^7 \text{ erg s}^{-1}$ $\equiv 10^{-7} W$ For other equivalents see units of power page 62
Magnetic Potential (V) (Magnetomotive force) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	I ampere $L^{1/2} M^{1/2} T^{-1} \mu_0^{-1/2}$ gilbert = $cm^{1/2} g^{1/2} s^{-1}$ $L^{3/2} M^{1/2} T^{-2} \epsilon_0^{1/2}$ $cm^{3/2} g^{1/2} s^{-2}$	A Gb esu	$\triangle 4\pi/10 Gb (= 1.2566 Gb) \triangle 4\pi c/10 esu$ (= $3.7673 \times 10^{10} esu$) $\triangle 10/4\pi A (= 7.9577 \times 10^{-1} A) \triangle c esu$ (= $2.9979 \times 10^{10} esu$) $\triangle 10/4\pi c A (= 2.6544 \times 10^{-11} A) \triangle 1/c emu$ (= $3.3357 \times 10^{-11} emu$)
Magnetic Field Strength (H) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	$L^{-1} I$ ampere/metre $L^{-1/2} M^{1/2} T^{-1} \mu_0^{-1/2}$ oersted* = $cm^{-1/2} g^{1/2} s^{-1}$ $L^{1/2} M^{1/2} T^{-2} \epsilon_0^{1/2}$ $cm^{1/2} g^{1/2} s^{-2}$	$A m^{-1}$ Oe* esu	$\triangle 4\pi/10^3 Oe (= 1.2566 \times 10^{-3} Oe) \triangle 4\pi c/10^3 esu$ (= $3.7673 \times 10^9 esu$) $\triangle 1 Gb cm^{-1} \triangle 10^3/4\pi A m^{-1} (= 7.9577 \times 10 A m^{-1})$ $\triangle 1 \text{ line of force per square centimetre}$ $\triangle c esu (= 2.9979 \times 10^{10} esu)$ $\triangle 10^3/4\pi c A m^{-1} (= 2.6544 \times 10^{-9} A m^{-1})$ $\triangle 1/c Oe (= 3.3357 \times 10^{-11} Oe)$
Magnetic Induction (B) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	$L^{-2} TU$ weber/square metre $L^{-1/2} M^{1/2} T^{-1} \mu_0^{1/2}$ gauss* = $cm^{-1/2} g^{1/2} s^{-1}$ $L^{-3/2} M^{1/2} \epsilon_0^{-1/2}$ $cm^{-3/2} g^{1/2}$	$Wb m^{-2}$ G* esu	$\triangle 10^4 \text{ gauss} \triangle 10^4/c esu (= 3.3357 \times 10^{-9} esu)$ $= 1 \text{ maxwell per cm}^2 \triangle 10^{-4} Wb m^{-2}$ $\triangle 1/c esu (= 3.3357 \times 10^{-11} esu)$ $\triangle 10^{-4} c Wb m^{-2} (= 2.9979 \times 10^4 Wb m^{-2})$ $\triangle c G (= 2.9979 \times 10^{10} G)$

* In geophysics the term gauss is used instead of oersted for the CGS-unit of magnetic field strength.

Electrical or Magnetic Quality (Symbol) Dimensional system System of measurement	Dimensions Unit	Symbol or abbreviation	Equivalents (\triangle indicates numerical but not dimensional equivalence c = velocity of light in a vacuum in centimetres per second = 2.9979×10^{10})
Absolute Permeability (μ_0) (Magnetic space constant, induction constant) Dimensional system LTUI Abs.el.syst.of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	$L^{-1} T U I^{-1}$ henry/metre μ_0 1 $L^{-2} T^2 \epsilon_0^{-1}$ $cm^{-2} s^2$	$H m^{-1}$ 1 [emu] esu	 $\triangle 10^7/4\pi$ [emu] (= 7.9577×10^5 [emu]) $\triangle 10^7/4\pi c^2$ esu (= 8.8550×10^{-18} esu) $\triangle 4\pi/10^7 H m^{-1}$ (= $1.2566 \times 10^{-6} H m^{-1}$) $\triangle 1/c^2$ esu (= 1.1127×10^{-21} esu) $\triangle 4\pi c^2/10^7 H m^{-1}$ (= $1.1294 \times 10^{15} H m^{-1}$) $\triangle c^2$ [emu] (= 8.9867×10^{20} [emu])
Magnetization (J) Dimensional system LTUI Abs.el.syst.of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	$L^{-1} I$ ampere/metre $L^{-1/2} M^{1/2} T^{-1} \mu_0^{-1/2}$ $cm^{-1/2} g^{1/2} s^{-1}$ $L^{1/2} M^{1/2} T^{-2} \epsilon_0^{1/2}$ $cm^{1/2} g^{1/2} s^{-2}$	$A m^{-1}$ emu esu	 $\triangle 10^{-3}$ emu $\triangle 10^{-3} c$ esu (= 2.9979×10^7 esu) $\triangle 10^3 A m^{-1} \triangle c$ esu (= 2.9979×10^{10} esu) $\triangle 10^3/c A m^{-1}$ (= $3.3357 \times 10^{-8} A m^{-1}$) $\triangle 1/c$ emu (= 3.3357×10^{-11} emu)
Magnetic Moment (M_m) Dimensional system LTUI Abs.el.syst.of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	$L^2 I$ ampere \times square metre $L^{5/2} M^{1/2} T^{-1} \mu_0^{-1/2}$ $cm^{5/2} g^{1/2} s^{-1}$ $L^{7/2} M^{1/2} T^{-2} \epsilon_0^{1/2}$ $cm^{7/2} g^{1/2} s^{-2}$	$A m^2$ emu esu	 $\triangle 10^3$ emu $\triangle 10^3 c$ esu (= 2.9979×10^{18} esu) $\triangle 10^{-3} A m^2 \triangle c$ esu (= 2.9979×10^{10} esu) $\triangle 10^{-3}/c A m^2$ (= $3.3357 \times 10^{-14} A m^2$) $\triangle 1/c$ emu (= 3.3357×10^{-11} emu)
Relative Magnetic Permeability (χ) Dimensional system LTUI Abs.el.syst.of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	1 1 1 1 1 1	 1 [Abs] 1 [emu] 1 (esu)	 $\triangle 1/4\pi$ [emu] (= 7.9577×10^{-9} [emu]) $\triangle 1/4\pi$ [esu] $\triangle 4\pi$ [Abs] (= 1.2566×10 [Abs]) \triangle [esu] $\triangle 4\pi$ [Abs] (= 1.2566×10 [Abs]) \triangle [emu]
Magnetic Pole Strength (m) Dimensional system LTUI Abs.el.syst.of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	LI ampere \times metre $L^{3/2} M^{1/2} T^{-1} \mu_0^{-1/2}$ $cm^{3/2} g^{1/2} s^{-1}$ $L^{5/2} M^{1/2} T^{-2} \epsilon_0^{1/2}$ $cm^{5/2} g^{1/2} s^{-2}$	$A m$ emu esu	 $\triangle 10$ emu $\triangle 10 c$ esu (= 2.9979×10^{11} esu) $\triangle 10^{-1} A m \triangle c$ esu (= 2.9979×10^{10} esu) $\triangle 10^{-1}/c A m$ (= $3.3357 \times 10^{-12} A m$) $\triangle 1/c$ esu (= 3.3357×10^{-11} emu)

Electrical or Magnetic Quality (Symbol) Dimensional system System of measurement	Dimensions Unit	Symbol or abbreviation	Equivalents (\triangle indicates numerical but not dimensional equivalence c = velocity of light in a vacuum in centimetres per second: = 2.9979×10^{10})
Magnetic Polarization (J) (Intensity of magnetization) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	$L^{-2} TU$ weber/square metre $L^{-1/2} M^{1/2} T^{-1} \mu_0^{1/2}$ $cm^{-1/2} g^{1/2} s^{-1}$ $L^{-3/2} M^{1/2} \epsilon_0^{-1/2}$ $cm^{-3/2} g^{1/2}$	$Wb\ m^{-2}$ emu esu	$\triangle 10^4/4\ \pi\ emu\ (= 7.9577 \times 10^2\ emu)$ $\triangle 10^4/4\ \pi\ c\ esu\ (= 2.6544 \times 10^{-8}\ esu)$ $\triangle 4\ \pi/10^4\ Wb\ m^{-2}\ (= 1.2566 \times 10^{-3}\ Wb\ m^{-2})$ $\triangle 1/c\ esu\ (= 3.3357 \times 10^{-11}\ esu)$ $\triangle 4\ \pi\ c/10^4\ Wb\ m^{-2}\ (= 3.7673 \times 10^7\ Wb\ m^{-2})$ $\triangle c\ emu\ (= 2.9979 \times 10^{10}\ emu)$
Magnetic Flux (Φ) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	TU weber (= Vs) $L^{3/2} M^{1/2} T^{-1} \mu_0^{1/2}$ maxwell = $cm^{3/2} g^{1/2} s^{-1}$ $L^{1/2} M^{1/2} \epsilon_0^{-1/2}$ $cm^{1/2} g^{1/2}$	Wb M esu	$\triangle 10^8\ M\ \triangle 10^8/c\ esu\ (= 3.3357 \times 10^{-3}\ esu)$ $\triangle 10^{-8}\ Wb\ \triangle 1/c\ esu\ (= 3.3357 \times 10^{-11}\ esu)$ $\triangle 10^{-8}\ c\ Wb\ (= 2.9979 \times 10^2\ Wb) = c\ M$ $(= 2.9979 \times 10^{10}\ M)$
Self-Inductance (L) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Electromagnetic CGS-system Dimensional system LMT ϵ_0 Electrostatic CGS-system	$TU I^{-1}$ henry = $V\ s\ A^{-1}$ $L\mu_0$ cm $L^{-1} T^2 \epsilon_0^{-1}$ $cm^{-1} s^2$	H emu (cm) esu	$\triangle 10^9\ emu\ (cm)\ \triangle 10^9/c^2\ esu\ (= 1.1127 \times 10^{-12}\ esu)$ $\triangle 10^{-9}\ H\ \triangle 1/c^2\ esu\ (= 1.1127 \times 10^{-21}\ esu)$ $\triangle 10^{-9}\ c^2\ H\ (= 8.9867 \times 10^{11}\ H)\ \triangle c^2\ emu$ $(= 8.9867 \times 10^{20}\ emu)$
Electrical or Magnetic Force (F) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Dimensional system LMT ϵ_0 Electromagnetic CGS-system Electrostatic CGS-system	$L^{-1} TUI$ Newton LMT^{-2} dyne = $cm\ g\ s^{-2}$	N dyn	$\equiv 10^5\ dyn$ $\equiv 10^{-5}\ N$ <div>For other equivalents see units of force, pages 59 and 60</div>
Electrical or Magnet. Energy (W) (Work) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Dimensional system LMT ϵ_0 Electromagnetic CGS-system Electrostatic CGS-system	TUI joule = $W\ s$ $\equiv A\ V\ s \equiv N\ m$ $\equiv m^2\ kg\ s^{-2}$ $L^2 MT^{-2}$ erg = $cm^2\ gs^{-2}$	J erg	$\equiv 10^7\ erg$ $\equiv 10^{-7}\ J$ <div>For other equivalents see units of energy, page 61</div>
Energy of Electromagnetic Radiation (S = POYNTING VECTOR) Dimensional system LTUI Abs. el. syst. of measurem. m-s-V-A Dimensional system LMT μ_0 Dimensional system LMT ϵ_0 Electromagnetic CGS-system Electrostatic CGS-system	$L^{-2} UI$ watt/square metre MT^{-3} erg/second \times square centimetre	$W\ m^{-2}$ erg $s^{-1}\ cm^2$	$= 10^3\ erg\ s^{-1}\ cm^2$ $= 10^{-3}\ W\ m^{-2}$

Units of radioactive decay

International unit: curie (c) = 10^3 millicuries (mc) = 10^6 microcuries (μ c).

The curie (formerly C) was originally defined as that quantity of radon (radium emanation) which is in radioactive equilibrium with 1 gram of radium. According to this definition, now obsolete, the curie corresponds to an activity of 3.71×10^{10} atoms disintegrating per second. In 1950 the *Joint Commission of the International Council of Scientific Unions on Standards, Units and Constants of Radioactivity* agreed upon a new, internationally recognized definition of the curie in order that a unit for the measurement of artificial radioactivity might also be available. The curie (c) is a radioactive unit; it is defined as that quantity of a radioactive nuclide in which 3.700×10^{10} disintegrations occur per second. The curie replaces the unit *rutherford* (rd = 10^6 disintegrations per second) proposed in 1946 by the U. S. National Bureau of Standards. The Joint Commission does not recognize the rutherford as an International unit.

Units of dosage for X-rays, gamma rays, and corpuscular radiation

X-rays and gamma rays¹

The international unit of dosage for X-rays and gamma rays is the röntgen (r), which is defined as that quantity of radiation which will produce in 0.001293 grams of air (= 1 ccm of air under normal conditions) a number of ions of both signs of charge corresponding to 1 esu each (electrostatic unit of electric charge) under conditions of elimination of the wall effects of the ionization chamber and complete exploitation of all secondary radiations. (Wave-length, intensity and duration are not taken into account in this definition.) A definition which is often more advantageous for the calculation of dosage may be derived from the following relationships which in turn are based upon the foregoing definition: The formation of ionic charges of both signs of 1 esu each per ccm of air corresponds to the production of 2.08×10^9 ion pairs (IP)/ccm of air = 1.61×10^{12} IP/gram of air. The formation of an ion pair in air by hard X-rays requires on the average an energy of $32.5 \text{ eV} = 52.065 \times 10^{-12}$ ergs. On the basis of the number of ion pairs produced in 1 gram of air by 1 r, the röntgen therefore corresponds to that quantity of radiation which distributes $1.61 \times 52.065 = 83.8$ ergs of energy in 1 gram of air:

$$\text{CGS-system: } 1 \text{ r} \triangleq 83.8 \text{ ergs/g}_{\text{air}} \triangleq 1.61 \times 10^{12} \text{ IP/g}_{\text{air}} = 774 \text{ esu/g}_{\text{air}}$$

$$\text{MKS-system: } 1 \text{ r} \triangleq 83.8 \times 10^{-4} \text{ J/kg}_{\text{air}} \triangleq 1.61 \times 10^{15} \text{ IP/kg}_{\text{air}} = 2.580 \times 10^{-4} \text{ C/kg}_{\text{air}}$$

In the exact computation of dosages, the unequal absorption of energy in air and in wet tissue (considered as water) must be taken into account:

$$1 \text{ r}_{\text{hard X-rays}} \triangleq 93 \text{ ergs/g}_{\text{tissue}} = 93 \times 10^{-4} \text{ J/kg}_{\text{tissue}}$$

The actual radiation output may be expressed as r/s or r/h:

$$1 \text{ r/s} \equiv 60 \text{ r/min} \equiv 3600 \text{ r/h} \triangleq 83.8 \text{ ergs s}^{-1}/\text{g}_{\text{air}} = 83.8 \times 10^{-4} \text{ W/kg}_{\text{air}}$$

$$\triangleq 93 \text{ ergs s}^{-1}/\text{g}_{\text{tissue}} = 93 \times 10^{-4} \text{ W/kg}_{\text{tissue}}$$

$$1 \text{ r/min} \equiv 60 \text{ r/h} \equiv 0.0166 \text{ r/s} \triangleq 1.396 \text{ ergs s}^{-1}/\text{g}_{\text{air}} = 1.396 \times 10^{-4} \text{ W/kg}_{\text{air}}$$

$$\triangleq 1.550 \text{ ergs s}^{-1}/\text{g}_{\text{tissue}} = 1.550 \times 10^{-4} \text{ W/kg}_{\text{tissue}}$$

$$1 \text{ r/h} \equiv 0.000277 \text{ r/s} \equiv 0.0166 \text{ r/min} \triangleq 0.0231 \text{ erg s}^{-1}/\text{g}_{\text{air}} = 2.31 \times 10^{-6} \text{ W/kg}_{\text{air}}$$

$$\triangleq 0.0258 \text{ erg s}^{-1}/\text{g}_{\text{tissue}} = 2.58 \times 10^{-6} \text{ W/kg}_{\text{tissue}}$$

Medical X-ray and gamma-ray units. The röntgen (r) is the sole internationally recognized unit. However, the skin erythema dose and the centimetre milligram-element hour (SIEVERT dose) have been and still are to some extent in use.

The *unit skin dose* or *skin erythema dose* (S.E.D.) is that quantity of X-rays or gamma rays which causes a slight reddening or browning of the skin in 80% of cases three weeks after irradiation. The absolute value of this unit is dependent on the wave-length of the radiation used, since the definition relates only to the energy which reaches and is absorbed by the surface of the skin. The conversion to röntgens is therefore also dependent upon the wave-length:

1 S.E.D. corresponds to 400–450 r of soft, or 525–600 r of medium hard, or 600–700 r of hard X-rays, or to 1000–1100 r of gamma rays (radium with products of disintegration).

1 r corresponds approximately to 0.00222–0.00250 S.E.D. of soft, or 0.00167–0.00190 S.E.D. of medium, or 0.00143 to 0.00167 S.E.D. of hard X-rays, or to 9.61×10^{-4} S.E.D. of gamma rays (radium with products of disintegration).

¹) X-rays are designated as those electromagnetic waves with a wave-length lying between approximately 10^{-11} and 10^{-8} cm. This range overlaps on one side the gamma rays (wave-length less than 10^{-11} cm) and on the other side the ultraviolet rays (wave-length between ca. 10^{-8} and 3.9×10^{-5} cm).

The *centimetre milligram-element hour* or millicurie of intensity/hour (Imch), now generally known as the *dose constant* (K) or SIEVERT dose, is employed only for the gamma rays of radium and corresponds to the application of one *millicurie of intensity* (Imc) during one hour. The Imc is defined as the radiation intensity of an elementary radium point source weighing 1 mg, filtered through 0.5 mm of platinum (absorption of corpuscular radiation), at a distance of 1 cm from the source.

$K \text{ (Imch)} = 8.2 \pm 0.2 \text{ r} = 0.0075\text{--}0.0084 \text{ S.E.D.}$ ($K = 7.5 \pm 0.2 \text{ r}$ when filtered through 1 mm of platinum).
1 r corresponds to 0.12–0.125 K; this corresponds to ca. 0.0009–0.001 S.E.D.

Corpuscular radiation

The unit of dose of corpuscular radiation is the *röntgen-equivalent physical* (rep). The rep is that quantity of radiation which will release an energy of 93 ergs per gram of tissue. Numerically it corresponds to the röntgen (r) in the energy definition per unit mass.

The (now rarely used) *röntgen-equivalent-man* (rem) is that quantity of radiation the biological effectiveness of which corresponds to that of one röntgen of hard X-rays.

The absorbed dose of any ionizing radiation is the amount of energy imparted to matter by ionizing particles per unit mass of irradiated material. It is expressed in *rad*. The *rad* is the unit of absorbed dose and is 100 ergs per gram (this unit was accepted by the International Commission on Radiological Units at the Copenhagen Conference in 1953).

The *gram-röntgen* is the product of the mass of irradiated material, expressed in grams, and the energy absorbed in that mass, expressed in rep:

$x \text{ gram}_{\text{tissue}} \cdot y \text{ abs. energy (rep)} = x \cdot y \text{ gram-röntgen.}$

For example, 10 gram-röntgen corresponds to the irradiation of 10 g of tissue with 1 rep, or to the irradiation of 1 g of tissue with 10 rep. The irradiation of larger tissue masses often involves high gram-röntgen values. The 10⁶ multiple of the gram-röntgen has therefore been introduced as a unit.

The integral absorbed dose is the integration of the energy absorbed throughout a given region:

Integral dose = x gram-röntgen or, applying the unit *rad*
Integral dose = x gram-rad, where 1 gram-rad = 100 ergs.

Since the biological activity of corpuscular radiation is very variable, the concept of *relative biological effectiveness* (r.b.e.) has been introduced. It is defined by comparison with the gamma radiation of radium filtered through 0.5 mm of platinum. Numerically it is the inverse ratio of the dose of the two radiations (in ergs per gram of tissue) required to produce the same biological effect under the same conditions. The following values are at present accepted:

	r.b.e.		r.b.e.
X-rays and γ -rays up to 3.0 MeV	1	Protons and deuterons	10
β -rays	1	Thermal neutrons	5
α -rays	20	Fast neutrons up to 20 MeV.....	10

Maximum permissible radiation doses (Tolerance doses)¹

The following table is based on the recommendations of the *International Commission on Radiological Protection*, Copenhagen, 1953. Cf. also *Dosimetry of radio-isotopes*, page 99.

	Maximum permissible weekly dose		
	X-rays and γ -rays up to 3 MeV r or rad	X-rays and γ -rays over 3 MeV r or rad	Any ionizing radiation rem
<i>Whole-body radiation</i>			
Haematogenic organs.....	} 0.3 ¹	} 0.3 ² for all parts of the body	} 0.3
Eyes			
Sex glands			
Basal layer of epidermis	0.6		0.6
<i>Partial radiation</i>			
Hands, forearms, feet, ankles, head, neck		1.5	1.5
Eyes		0.3 ³	—

¹⁾ The hourly tolerance dose on a 48-hour working week is 6.25 mr/h.
²⁾ This dose should be measured at the peak of the transition curve in tissue or in a tissue-equivalent phantom.
³⁾ Particular care should be taken to protect the eyes and a maximum weekly dose of 0.15 r or rad should be adhered to as far as possible.

Quality	Units	Symbol or abbreviation
<p>The luminous flux Φ is the photometrically evaluated radiation of light. The bases for its evaluation are the <i>relative spectral sensitivity</i> $(V_\lambda)^1$ of the eye adapted to bright light and the mechanical equivalent of light $(M)^2$.</p>	lumen	lm
<p>The quantity of light Q is the product of the luminous flux and its duration.</p>	<div><div>{</div><div>lumen second lumen hour</div></div>	<div><div>lm s lm h</div></div>
<p>The luminous intensity I in a given direction is the relation between the luminous flux radiated in that direction and the area upon which it falls, i.e. luminous flux per unit area. The unit is the <i>candela</i> or international candle³. A source of light having a luminous intensity of one candela in all directions produces a luminous flux of 4π lm.</p>	candela	cd
<p>The luminance (brightness) L of a surface in a given direction is the ratio of the luminous intensity in that direction to the orthogonal projection of the radiating surface in that direction.</p>	<div><div>{</div><div>stilb \equiv cd/cm² apostilb \equiv sb/10⁴ π lambert \equiv sb/$\pi \equiv$ 10⁴ asb</div></div>	<div><div>{</div><div>sb asb La</div></div>
<p>The unit of brightness for scotopic vision, in contrast to the preceding units, is related to the eye adapted to vision in the dark (rod vision). The conversion factor between this and the luminance L depends on the composition of the light. The unit is used only up to 10 skot.</p>	<div>skot = 10⁻³ asb for radiation with a colour temperature of 2360°K</div>	sk
<p>The specific luminous radiation H of a surface is the ratio of the radiated luminous flux to the area of the surface.</p>	phot ⁴ \equiv lm/cm ²	ph
<p>The intensity of illumination E is the ratio of the luminous flux incident upon a surface to the area A of the surface, $E = \Phi/A$, and therefore corresponds to the specific radiation with respect to that part of the radiation reaching the surface illuminated. 1 lm uniformly distributed over 1 m² of surface produces an intensity of 1 lux.</p>	lux \equiv lm/m ²	lx
<p>The unit of intensity of illumination for scotopic vision is analogous to that of brightness for scotopic vision, and relates to the eye adapted to vision in the dark.</p>	<div>nox = 10⁻³ lx for radiation with a colour temperature of 2360°K</div>	nx
<p>The quantity of illumination is the product of the intensity of illumination and its duration.</p>	lux second	lx s
<p>The luminous efficiency of a source of light is the ratio of the total luminous flux emitted to the power absorbed.</p>	lumen/watt	lm/W

¹⁾ For the relative spectral sensitivity of the eye V_λ the following internationally recognized values are used (λ = wave-length of light in m μ):

λ	V_λ	λ	V_λ	λ	V_λ	λ	V_λ	λ	V_λ	λ	V_λ	λ	V_λ	λ	V_λ
400	0.0004	440	0.023	480	0.139	520	0.710	555	1.000	590	0.757	630	0.265	670	0.032
410	0.0012	450	0.038	490	0.208	530	0.862	560	0.995	600	0.631	640	0.175	680	0.017
420	0.0040	460	0.060	500	0.323	540	0.954	570	0.952	610	0.503	650	0.107	690	0.0082
430	0.0116	470	0.091	510	0.503	550	0.995	580	0.870	620	0.381	660	0.061	700	0.0041
														710	0.0021
														720	0.00105
														730	0.00052
														740	0.00025
														750	0.00012
														760	0.00006

²⁾ The mechanical or electrical equivalent of light M is calculated for the lumen based on the candela as $M = (1.46_7 \pm 0.010) \times 10^{-3} \text{ J} \times (\text{s} \times \text{lm})^{-1} = (1.46_7 \pm 0.010) \times 10^{-3} \text{ W/lm}$, or $1/M = (680 \pm 5) \text{ lm/W}$. The new lumen corresponds, therefore, to a radiation of 0.00146 W.

³⁾ The candela is defined by the condition that the luminance L of a black-body radiator should amount to 60 candela per square centimetre at the temperature of solidifying platinum.

⁴⁾ The phot, which by definition is the unit of specific radiation, is frequently used as a unit of illumination. 1 phot then = 10⁴ lux.

Quality and definition	Dimension	Units	
		MKS-Equivalent	CGS-Equivalent
Velocity of sound This is the velocity with which sound vibrations are propagated in a medium. Within the range of audible sound this velocity is the same for all frequencies. In gases and liquids sound assumes the form of a longitudinal wave; in solid bodies both longitudinal and transverse waves may occur.	LT ⁻¹	m s ⁻¹	cm s ⁻¹
Frequency of sound (Tone frequency) This represents the number of sound vibrations per unit of time.	T ⁻¹	Hz	Hz
Wave-length The wave-length of sound is the velocity of sound divided by its frequency.	L	m	cm
Sound pressure This is the oscillating pressure produced by sound vibrations.	L ⁻¹ MT ⁻²	N m ⁻²	dyn cm ⁻² (≡ μb)
Sound intensity or strength The intensity of sound at a given point is the amount of vibratory energy flowing through unit cross-sectional area per unit of time.	MT ⁻³	W m ⁻²	erg s ⁻¹ cm ⁻²
Sound output Sound output is the vibratory energy flowing per unit of time through a surface which encloses the source of the sound.	L ² MT ⁻³	W	erg s ⁻¹
Loudness	1	phon	phon
Relative loudness Damping, amplification	1	decibel (db)	decibel (db)

The **loudness of sound** is defined as the sensation of sound ("audible" sound pressure) produced by a given sound pressure. Since the audibility is dependent upon the frequency (maximum sensitivity at approximately 1000 to 2000 vibrations per second), sounds of equal sound pressure but unequal frequency result in different loudnesses. The curve of audibility is flatter at high sound pressures than at low.

The loudness (*L*) of a sound is the ratio of its pressure (*p*) to the standard sound pressure of a tone at the auditory threshold of 1000 vibrations per second (*p*₀ = 2 × 10⁻⁴ μb). In accordance with the WEBER-FECHNER Law (logarithmic dependence of the auditory sensation on the energy of excitation) loudness is not expressed directly by the ratio *p/p*₀ but by the 20th multiple of the logarithm of this ratio. The unit so derived is called the phon:

*L*_{phon} = 20 log₁₀ *p* (in μb)/2 × 10⁻⁴ μb. The phon scale, therefore, is a logarithmic scale of dimensionless ratios. Since the denominator of the quotient (= sound pressure of the auditory threshold = 2 × 10⁻⁴ μb), and therefore also the phon scale, are fixed, the sound pressure is determined by the corresponding loudness expressed in phons:

$$x \text{ phons} \triangleq 0.0002 \times 10^{0.05x} \mu b$$

The human ear responds to sound pressures ranging from approximately 630 μb (threshold of pain) to 0.0002 μb (auditory threshold). This corresponds to a sound pressure ratio of 10^{6.5}:10 or to a sound intensity ratio of 10¹³:10 or 130 phons:

Phons	Corresponding value in microbars (μb)	Corresponding noise	Phons	Corresponding value in microbars (μb)	Corresponding noise
0	0.0002 × 10 ⁰ = 0.0002	auditory threshold	70	0.0002 × 10 ^{3.5} = 0.6324	traffic in a busy street
1	0.0002 × 10 ^{0.05} = 0.0002244		80	0.0002 × 10 ⁴ = 2	heavy traffic
10	0.0002 × 10 ^{0.5} = 0.0006324	soft whispering, ticking of pocket watch	90	0.0002 × 10 ^{4.5} = 6.324	motor cycle with silencer
20	0.0002 × 10 ¹ = 0.002	noise in a quiet dwelling	100	0.0002 × 10 ⁵ = 20	loudest motor horn
30	0.0002 × 10 ^{1.5} = 0.006324	rustling of trees, quiet street	110	0.0002 × 10 ^{5.5} = 63.24	working of sheet iron
40	0.0002 × 10 ² = 0.02	tearing of writing paper	120	0.0002 × 10 ⁶ = 200	aeroplane propeller, riveting
50	0.0002 × 10 ^{2.5} = 0.06324	conversational speech	130	0.0002 × 10 ^{6.5} = 632.4	threshold of auditory pain
60	0.0002 × 10 ³ = 0.2	tramcar			

The **decibel (db)** is used to express **relative loudness**. Like the phon it is the 20th multiple of the logarithm of a dimensionless ratio of two sound pressures which are to be compared. However, the denominator of the quotient and therefore also the decibel scale are not fixed: *L*_{db} = 20 log₁₀ *p/p*₁ (*p*₁ = initial sound pressure, *p* = sound pressure being compared). The gain or loss of loudness, expressed in db, is therefore: ± *x* db = 10^{± 0.05 *x*}. Example: an increase in sound pressure from *p*₁ to *p* = 10^{0.05}*p*₁ corresponds to a gain in loudness of +1 db, a decrease in sound pressure from *p*₁ to *p* = 10⁻¹*p*₁ corresponds to a loss of loudness of -20 db.

Tone Scales

The tone scales are built up on the basis of definite frequency ratios between the tones and in a manner appropriate to the musical sensitivity of the human ear. The most important tone intervals are arranged according to consonance and dissonance:

Consonant tone interval	Frequency ratio	Dissonant tone interval	Frequency ratio
Twelfth	3:1	Major seventh ...	15:8
Octave	2:1	Minor seventh ...	9:5
Major sixth	5:3	Minor sixth	8:5
Fifth	3:2	Major whole tone .	9:8
Fourth	4:3	Minor whole tone .	10:9
Major third	5:4	Major semitone ..	16:15
Minor third	6:5	Minor semitone ..	25:24
Unison	1:1		

The border-line between consonance and dissonance is fluid and shows a tendency to shift in time in favour of those intervals which were formerly felt to be dissonant, such as, for instance, the minor sixth and minor seventh.

A distinction, based on the manner in which the tone scales are built up, is drawn between *diatonic* and *chromatic* scales. In the case of the diatonic major or minor scale 7 notes are distributed unequally over the octave:

Diatonic major scale		
Tone interval	Note symbol	Frequency ratio
First	C	1
Second	D	10:9
Major third	E	5:4
Fourth	F	4:3
Fifth	G	3:2
Major sixth	A	5:3
Major seventh	B	15:8
Octave	C'	2

Diatonic minor scale		
Tone interval	Note symbol	Frequency ratio
First	C	1
Second	D	10:9
Minor third	E flat	6:5
Fourth	F	4:3
Fifth	G	3:2
Minor sixth	A flat	8:5
Minor seventh	B	9:5
Octave	C'	2

In the case of the chromatic scale 12 semitones are distributed equally (equal temperament) over the octave, each semitone having $\sqrt[12]{2}$ times the frequency of the previous one:

Chromatic scale			
Note symbol	Frequency ratio	Note symbol	Frequency ratio
C	1	G	$2^{7/12}$
C sharp = D flat	$2^{1/12}$	A flat = G sharp	$2^{8/12}$
D	$2^{2/12}$	A	$2^{9/12}$
D sharp = E flat	$2^{3/12}$	B flat = A sharp	$2^{10/12}$
E = F flat	$2^{4/12}$	B = C' flat	$2^{11/12}$
F = E sharp	$2^{5/12}$	C' = B sharp	$2^{12/12}$
F sharp = G flat	$2^{6/12}$		

These divisions of the tone scale hold good for any octave range whatever and are independent of the absolute value of the basic note of the scale. The pitch of the tone scale is fixed by the frequency of the note C = $2^4 \times 16$ cps = 256 cps.

The 12-interval chromatic scale is fixed by the pitch of the note A. From 1859 to 1939 the French concert-pitch $a' = 435$ cps (agreed upon at the Vienna tuning pitch conference in 1885) was accepted as the standard. In 1939 the international committee of the ISA in London fixed the standard pitch at 440 cps. The frequencies of the 12-interval chromatic scale, which is today internationally accepted, are therefore:

Vibration frequencies of the 12-interval chromatic scale, A = 440.0 cps

	c^{-3}	c^{-2}	c^{-1}	c^0	c^1	c^2	c^3	c^4	Ratios
C	16.35	32.70	65.41	130.81	261.63	523.25	1046.50	2093.00	1.00000
C \sharp D \flat	17.32	34.65	69.30	138.59	277.18	554.37	1108.73	2217.46	$\sqrt[12]{2} = 1.05946$
D	18.35	36.71	73.42	146.83	293.66	587.33	1174.66	2349.32	$\sqrt[12]{2^2} = 1.12246$
D \sharp E \flat	19.45	38.89	77.78	155.56	311.13	622.25	1244.51	2489.02	$\sqrt[12]{2^3} = 1.18921$
E	20.60	41.20	82.41	164.81	329.63	659.26	1318.51	2637.02	$\sqrt[12]{2^4} = 1.25992$
F	21.83	43.65	87.31	174.61	349.23	698.46	1396.91	2793.83	$\sqrt[12]{2^5} = 1.33484$
F \sharp G \flat	23.12	46.25	92.50	185.00	369.99	739.99	1479.98	2959.96	$\sqrt[12]{2^6} = 1.41421$
G	24.50	49.00	98.00	196.00	392.00	783.99	1567.98	3135.96	$\sqrt[12]{2^7} = 1.49831$
G \sharp A \flat	25.96	51.91	103.83	207.65	415.30	830.61	1661.22	3322.44	$\sqrt[12]{2^8} = 1.58740$
A	27.50	55.00	110.00	220.00	440.00	880.00	1760.00	3520.00	$\sqrt[12]{2^9} = 1.68179$
A \sharp B \flat	29.14	58.27	116.54	233.08	466.16	932.33	1864.66	3729.31	$\sqrt[12]{2^{10}} = 1.78180$
B	30.87	61.74	123.47	246.94	493.88	987.77	1975.53	3951.07	$\sqrt[12]{2^{11}} = 1.88775$
									$(\log_{10} \sqrt[12]{2} = 0.025085832972)$

$c^{-3} = C_2$ = subcontra-octave; $c^{-2} = C_1$ = contra-octave; $c^{-1} = C$ = great octave; $c^0 = c$ = small octave; $c^1 = c'$ = one-line octave; $c^2 = c''$ = two-line octave; etc. Only the organ can cover the whole range c^{-3} to c^5 (c^5 = frequency of 4186.0).

Fundamental Chemical Mass Units

Mass of *N* molecules or atoms of a chemically homogeneous substance

(*N* = AVOGADRO's number¹)

This is equal to the molecular or atomic weight of the given substance multiplied by the unit of mass.
Dimension in the LMT-systems = M

Units in the derived systems of measurement:

- CGS-system²: mole (mol) = (molecular or atomic weight of the substance) × grams
- MKS-system²: kilomole (kmol) = (molecular or atomic weight of the substance) × kilograms
- 1 mol = 10⁻³ kmol = 10³ mmol = 10⁶ μmol; 1 kmol = 10³ mol = 10⁶ mmol = 10⁹ μmol

As a result of the difference between the physical and chemical scales of atomic weights, there are two slightly different values for moles:

mole _{chemical scale}	corresponds to the mass of <i>N</i> molecules or atoms ¹ , <i>N</i> =	is equal to: mole _{physical scale}	corresponds to the mass of <i>N</i> molecules or atoms ¹ , <i>N</i> =
mol _{ch.sc.}	6.023 × 10 ²³	1.000279 mol _{ph.sc.}	6.025 × 10 ²³
kmol _{ch.sc.}	6.023 × 10 ²⁶	1.000279 kmol _{ph.sc.}	6.025 × 10 ²⁶

Mass of *N*/*z* ions of a chemically homogeneous substance

(*N* = AVOGADRO's number¹, *z* = valency of the given ions)

This is equal to (molecular or atomic weight of the given ions/valency) multiplied by the unit of mass.
Dimension in the LMT-systems = M

Units in the derived systems of measurement:

- CGS-system: gram equivalent or equivalent (equ. or equiv or g. equiv)³
= (molecular or atomic weight of the given ions/valency) × grams = mol/valency
- MKS-system: kilogram equivalent (kg. equiv)³ = (molecular or atomic weight of the given ions/valency) × kilograms
= kmol/valency
- 1 g. equiv = 10⁻³ kg. equiv = 10³ mg. equiv; 1 kg. equiv = 10³ g. equiv = 10⁶ mg. equiv

As a result of the difference between the physical and chemical scales of atomic weights, there are two slightly different values for equivalents:

equivalent _{chemical scale}	carries an electric charge of ⁴	is equal to: equivalent _{physical scale}	carries an electric charge of ⁴
1 g. equiv _{ch.sc.}	9.6498 × 10 ⁴ C △ 2.8929 × 10 ¹⁴ esu	1.000279 g. equiv _{ph.sc.}	9.6525 × 10 ⁴ C △ 2.8937 × 10 ¹⁴ esu
1 kg. equiv _{ch.sc.}	9.6498 × 10 ⁷ C △ 2.8929 × 10 ¹⁷ esu	1.000279 kg. equiv _{ph.sc.}	9.6525 × 10 ⁷ C △ 2.8937 × 10 ¹⁷ esu

¹) AVOGADRO's number *N* is the numerical value of AVOGADRO's constant *N_A*. In German-speaking countries it is known as LOSCHMIDT's number and the expression AVOGADRO's number is in general used to represent the number of molecules contained in 1 ccm of a perfect gas at normal temperature and pressure. (Cf. Physical constants, page 79.)

²) The designation gram mole instead of mole is also used. For atoms the designations gram atom (g. atom) and kilogram atom (kg. atom) are usually employed.

³) Internationally recognized symbols for gram equivalent and kilogram equivalent are val and kval respectively.

⁴) This charge is known as the *faraday*, and is defined as the charge carried by a quantity of ions having a mass of 1 g. equiv (CGS-system) or 1 kg. equiv (MKS-system).

Analytical Units

Mass/Mass

Designation	Symbol	Definition
Solids		
Mass per cent	% (weight %)	Grams of the substance contained in 100 grams of total mass
Milligram per cent ¹	mg%	Milligrams of the substance contained in 100 grams of total mass
Mole per cent	mol%	Used particularly in connection with isomorphic mixtures, fused mixtures, etc.
Solutions		
Mass per cent	% (weight %)	Grams of solute contained in 100 grams of solution
	g/100 g solvent	Grams of solute contained in 100 grams of solvent
	mg%	Milligrams of solute contained in 100 grams of solution ¹
	mol/100 g solution	Mole, g. atom or g. equiv of solute in 100 grams of solution, etc.
	g. atom/100 g solution .	
	g. equiv/100 g solution .	
	etc.	
	mol/100 g solvent	Mole, g. atom or g. equiv of solute in 100 grams of solvent, etc.
	g. atom/100 g solvent ..	
	g. equiv/100 g solvent ..	
	etc.	
Molecular or molar ratio	mol%	Moles of solute in 100 moles of solution
	mol ‰	Millimoles of solute in 1 mole of solution or moles of solute in 1000 moles of solution
	mol/100 mol solvent	Moles of solute in 100 moles of solvent
	mol/1000 mol solvent ...	Moles of solute in 1000 moles of solvent
Dilution	g solvent/1 g solute	Grams of solvent per gram of solute
	mol solvent/1 mol solute .	Moles of solvent per mole of solute
Molality	mol/1000 g solvent	moles } of solute in 1000 grams of solvent gram atoms }
	g. atom/1000 g solvent ..	
Gases		
Mass per cent	% (weight %)	Grams of the gas in question in 100 grams of gas mixture
Mole per cent	mol%	Moles of the gas in question in 100 moles of all components

Mass/Volume²

Solutions		
	g/100 ml solution	Grams of solute in 100 ml of solution
	mg%	Milligrams of solute in 100 ml of solution ¹
	g/l	Grams of solute in 1 litre of solution
	g/100 ml	Grams of solute in 100 ml of solution
	g/100 ml solvent	Grams of solute in 100 ml of solvent
	mol/l	moles } of the substance in 1 litre of solution (0.1-M, 0.01-M, etc.) gram atoms }
	g. atom/l	
	N	Gram equivalents of the solute in 1 litre of solution (0.1-N, 0.01-N, etc.)
	g. equiv/l	

Volume/Volume

Volume per cent	vol%	Millilitres of solute in 100 ml of solution or cubic centimetres of gas in 100 ml of solution or cubic centimetres of gas in 100 ccm of gas mixture
-----------------------	------------	-----------------------------------------------------------------------------------------------------------------------------------------------------------

¹⁾ The expression mg% is an unfortunate one inasmuch as the units concerned are not clearly specified. In medical literature it is used equally to mean mg/100 g and mg/100 ml, particularly with reference to blood, urine, etc. For this reason the use of the expression mg% has been avoided in these Tables.

²⁾ Dependent upon temperature.

(*World Hlth Org. techn. Rep. Ser.*, 56, 20, 1952; 68, 5, 1953; 86, 5, 1954; *Pharmacopoea Internat.*, Vol. II, Geneva, 1955, pp. 254–260)

Preparation	Adopted ³	Reference	Unit ³ mg	Form in which dispensed
A. Held by the Department of Biological Standards, National Serum Institute, Copenhagen				
Antitoxins and Antisera				
Anti- <i>Brucella abortus</i> ⁴	1952	<i>World Hlth Org. techn. Rep. Ser.</i> , 68, 9, 1953	0.091	Ampoules containing 91 mg
Antidysentery serum (<i>Shigella dysenteriae</i> SHIGA)	1928	<i>Quart. Bull. Hlth Org. L. o. N.</i> , 5, 728, 1936	0.0500	In glycerol (66 vol%), 200 I.U./l Bottles containing ca. 8 ml
Antipneumococcus serum (type I)	1934	<i>Quart. Bull. Hlth Org. L. o. N.</i> , 4, 5, 1935	0.0886	In glycerol (66 vol%), 200 I.U./l Bottles containing ca. 10 ml
Antipneumococcus serum (type II)	1934	<i>Quart. Bull. Hlth Org. L. o. N.</i> , 4, 6, 1935	0.0894	In glycerol (66 vol%), 200 I.U./l Bottles containing ca. 10 ml
Anti-Q-fever serum ⁴	1953	<i>World Hlth Org. techn. Rep. Ser.</i> , 86, 10, 1954	0.1017	Ampoules containing ca. 0.1 g dried serum
Antityphoid serum (P.I.S.)	1952	<i>World Hlth Org. techn. Rep. Ser.</i> , 68, 10, 1953	—	Ampoules containing 5 ml dried serum
Cholera agglutinating serum (INABA) (I.R.P.)	1953	<i>World Hlth Org. techn. Rep. Ser.</i> , 86, 7, 1954	—	Ampoules containing 0.6 ml
Cholera agglutinating serum (OGAWA) (I.R.P.)	1953	<i>World Hlth Org. techn. Rep. Ser.</i> , 86, 7, 1954	—	Ampoules containing 0.6 ml
<i>Clostridium welchii</i> (perfringens) Type B antitoxin (I.R.P.)	1954	<i>World Hlth Org. techn. Rep. Ser.</i> , 96, 6, 1955	0.0137	Ampoules containing ca. 69 mg
<i>Clostridium welchii</i> (perfringens) Type D antitoxin (I.R.P.)	1954	<i>World Hlth Org. techn. Rep. Ser.</i> , 96, 6, 1955	0.0657	Ampoules containing ca. 66 mg
Diphtheria antitoxin	1922	<i>Quart. Bull. Hlth Org. L. o. N.</i> , 5, 728, 1936	0.0628	In glycerol (66 vol%), 10 I.U./ml Bottles containing ca. 10 ml
Diphtheria antitoxin for flocculation test	1935	<i>Quart. Bull. Hlth Org. L. o. N.</i> , 5, 577, 1936; <i>Bull. Hlth Org. L. o. N.</i> , 7, 712, 1938	—	Dilution of hyperimmune horse serum in phosphate-buffered saline containing 0.01 g/100 ml of thiomersal (merthio- late, sodium ethylmercurithiosalicylate), 500 I.U./ml. Bottles containing ca. 10 ml
Gas-gangrene antitoxin (histolyticus)	1935	<i>World Hlth Org. techn. Rep. Ser.</i> , 56, 17, 1952	0.2000	In glycerol (66 vol%), 20 I.U./ml Bottles containing ca. 5 ml
Gas-gangrene antitoxin (oedematiens)	1934	<i>Quart. Bull. Hlth Org. L. o. N.</i> , 4, 3, 1935; <i>Bull. Hlth Org. L. o. N.</i> , 10, 97, 1942–43	0.2681	In glycerol (66 vol%), 20 I.U./ml Bottles containing ca. 5 ml
Gas-gangrene antitoxin (perfringens) ⁵	1931	<i>Bull. Hlth Org. L. o. N.</i> , 10, 97, 1942–43	0.1132	In glycerol (66 vol%), 20 I.U./ml Bottles containing ca. 5 ml
Gas-gangrene antitoxin (Sordelli)	1938	<i>Bull. Hlth Org. L. o. N.</i> , 7, 698, 1938; 8, 856, 1939	0.1334	In glycerol (66 vol%), 20 I.U./ml Bottles containing ca. 10 ml
Gas-gangrene antitoxin (vibrio septique)	1934	<i>Bull. Hlth Org. L. o. N.</i> , 10, 97, 1942–43; <i>Bull. World Hlth Org.</i> , 1, 9, 1947–48	0.0974	In glycerol (66 vol%), 50 I.U./ml Bottles containing ca. 5 ml
Scarlet fever streptococcus antitoxin	1952	<i>World Hlth Org. techn. Rep. Ser.</i> , 68, 11, 1953	0.049	Ampoules containing 490 mg
Staphylococcus α antitoxin	1934	<i>Quart. Bull. Hlth Org. L. o. N.</i> , 4, 7, 1935; <i>Bull. Hlth Org. L. o. N.</i> , 7, 704, 1938	0.2376	In phosphate-buffered saline containing 0.01 g/100 ml thiomersal (merthiolate, sodium ethylmercurithiosalicylate), 20 I.U./ml. Bottles containing ca. 5 ml
Staphylococcus β antitoxin	1952	<i>World Hlth Org. techn. Rep. Ser.</i> , 68, 11, 1953	2.623	In phosphate-buffered saline containing 0.01 g/100 ml thiomersal (merthiolate, sodium ethylmercurithiosalicylate), 20 I.U./ml. Bottles containing ca. 5 ml
Swine erysipelas serum (anti-N)	1954	<i>World Hlth Org. techn. Rep. Ser.</i> , 96, 10, 1955	—	Ampoules containing ca. 88 mg
Tetanus antitoxin	1928	<i>World Hlth Org. techn. Rep. Ser.</i> , 2, 5, 1950	0.3094	In glycerol (66 vol%), 5 I.U./ml Bottles containing ca. 10 ml
Blood-Typing Sera				
Anti-A blood-typing serum	1950	<i>Bull. World Hlth Org.</i> , 3, 301, 1950	0.3465	Ampoules containing ca. 90 mg
Anti-B blood-typing serum	1950	<i>Bull. World Hlth Org.</i> , 3, 301, 1950	0.3520	Ampoules containing ca. 90 mg

¹) Additional references, and a historical account of standards adopted before 1945, may be found in GAUTIER, R., *Quart. Bull. Hlth Org. L. o. N.*, 4, 497, 1935; GAUTIER, R., *Bull. Hlth Org. L. o. N.*, 12, 1, 1945–46.

²) Provisional International Standards are indicated by (P.I.S.) after the name of the substance; International Reference Preparations by (I.R.P.); and Provisional International Reference Preparations by (P.I.R.P.). All the other substances listed have the full status of International Biological Standards.

³) The date refers to the adoption of the *First* International Standard for each substance, while the unitage is that of the *current* standard.

⁴) Also held by the Ministry of Agriculture and Fisheries Veterinary Laboratory, Weybridge, England.

⁵) See also *Clostridium welchii* (perfringens).

Preparation	Adopted	Reference	Unit mg	Form in which dispensed
Antigens, etc.				
Cardiolipin (P.I.R.P.)	1951	<i>World Hlth Org. techn. Rep. Ser.</i> , 56, 8, 1952	—	7.2 mg/ml. Bottles containing 10 ml
Cholera antigen (INABA) (I.R.P.)	1953	<i>World Hlth Org. techn. Rep. Ser.</i> , 86, 7, 1954	—	Ampoules containing 100 mg
Cholera antigen (OGAWA) (I.R.P.)	1953	<i>World Hlth Org. techn. Rep. Ser.</i> , 86, 7, 1954	—	Ampoules containing 100 mg
Cholera vaccine (INABA) (I.R.P.)	1953	<i>World Hlth Org. techn. Rep. Ser.</i> , 86, 7, 1954	—	Ampoules containing 20 mg
Cholera vaccine (OGAWA) (I.R.P.)	1953	<i>World Hlth Org. techn. Rep. Ser.</i> , 86, 7, 1954	—	Ampoules containing 20 mg
Diphtheria toxoid, plain	1951	<i>World Hlth Org. techn. Rep. Ser.</i> , 56, 4, 1952	—	Awaiting decision on unitage Ampoules containing ca. 50 mg
Lecithin (beef heart) (I.R.P.)	1951	<i>World Hlth Org. techn. Rep. Ser.</i> , 56, 8, 1952	—	30 mg/ml. Bottles containing 30 ml
Lecithin (egg) (P.I.R.P.)	1951	<i>World Hlth Org. techn. Rep. Ser.</i> , 56, 8, 1952	—	30.2 mg/ml. Bottles containing 30 ml
Old tuberculin	1931	<i>Quart. Bull. Hlth Org. L. o. N.</i> , 5, 728, 1936; <i>Off. Rec. World Hlth Org.</i> , 11, 10, 1948	0.0100	100,000 I.U./ml Ampoules containing ca. 2 ml
Purified protein derivative of mammalian tuberculin	1951	<i>World Hlth Org. techn. Rep. Ser.</i> , 56, 6, 1952	0.000028	Ampoules containing ca. 10 mg plus 4 mg of salts
Purified protein derivative of avian tuberculin	1954	<i>World Hlth Org. techn. Rep. Ser.</i> , 96, 11, 1955	0.0000726	Ampoules containing ca. 10 mg plus 26 mg of salts
SCHICK-test toxin (diphtheria)	1954	<i>World Hlth Org. techn. Rep. Ser.</i> , 96, 7, 1955	—	Ampoules containing ca. 3.8 mg
Tetanus toxoid	1951	<i>World Hlth Org. techn. Rep. Ser.</i> , 56, 5, 1952	0.0300	Ampoules containing ca. 25 mg
Opacity reference preparation (I.R.P.)	1953	<i>World Hlth Org. techn. Rep. Ser.</i> , 86, 14, 1954	—	Ampoules containing 20 ml

B. Held by the Department of Biological Standards, National Institute for Medical Research, London

Vitamins				
Provitamin A (pure β-carotene)	1949	<i>World Hlth Org. techn. Rep. Ser.</i> , 3, 6, 1950	0.0006	In vegetable oil, 200 I.U./g Bottles containing ca. 10 g
Vitamin B (pure synthetic vitamin B ₁)	1934	<i>Quart. Bull. Hlth Org. L. o. N.</i> , 3, 435, 1934; <i>Bull. Hlth Org. L. o. N.</i> , 7, 882, 1938	0.003	Ampoules containing ca. 20 mg
Vitamin C (L-ascorbic acid)	1934	<i>Quart. Bull. Hlth Org. L. o. N.</i> , 3, 436, 1934	0.05	Ampoules containing ca. 550 mg
Vitamin D (pure vitamin D ₃)	1931	<i>World Hlth Org. techn. Rep. Ser.</i> , 3, 7, 1950; <i>Bull. World Hlth Org.</i> , 10, 875, 1954	0.000025	In vegetable oil, 1000 I.U./g Bottles containing ca. 10 g
Vitamin E (α-tocopheryl acetate)	1941	<i>Bull. Hlth Org. L. o. N.</i> , 9, 443, 1940–41	1.0	In olive oil, 10 I.U./g Bottles containing ca. 10 g

Hormones, Protamines, etc.				
Adrenocorticotropic hormone, ACTH (active principle from pig pituitary, dried)	1950	<i>World Hlth Org. techn. Rep. Ser.</i> , 36, 7, 1951	1.0	Ampoules containing ca. 1.3 mg and 5.0 mg
Chorionic gonadotropin (active principle from human urine of pregnancy, dried and diluted with lactose)	1939	<i>Bull. Hlth Org. L. o. N.</i> , 8, 884, 1939	0.1	Ampoules containing twenty-five 10-mg tablets
Serum gonadotropin (active principle from serum of pregnant mares, dried and diluted with lactose)	1939	<i>Bull. Hlth Org. L. o. N.</i> , 8, 898, 1939	0.25	Ampoules containing ten 25-mg tablets
Heparin (dried sodium salt)	1942	<i>Bull. Hlth Org. L. o. N.</i> , 10, 151, 1942–43; <i>Bull. World Hlth Org.</i> , 1, 7, 1947–48	0.0077	Ampoules containing ca. 50 mg
Insulin (pure crystalline)	1935	<i>Bull. World Hlth Org.</i> , 7, 445, 1952	0.04082	Ampoules containing ca. 20 mg
Pituitary, posterior lobe powder	1935	<i>Quart. Bull. Hlth Org. L. o. N.</i> , 5, 572, 1936; <i>Bull. Hlth Org. L. o. N.</i> , 10, 89, 1942–43	0.5	Ampoules containing ca. 30 mg
Prolactin	1939	<i>Bull. Hlth Org. L. o. N.</i> , 8, 909, 1939	0.1	Ampoules containing ten 10-mg tablets
Progesterone	1935	<i>Quart. Bull. Hlth Org. L. o. N.</i> , 4, 628, 1935; <i>Bull. Hlth Org. L. o. N.</i> , 10, 86, 1942–43	1.0	Ampoules containing ca. 65 mg
Protamine	1954	<i>World Hlth Org. techn. Rep. Ser.</i> , 96, 14, 1955	—	Ampoules containing ca. 60 mg
Thyrotropin	1954	<i>World Hlth Org. techn. Rep. Ser.</i> , 96, 14, 1955	—	Ampoules containing ten 20-mg tablets

Preparation	Adopted	Reference	Unit mg	Form in which dispensed
Glycosides and Alkaloids				
Digitalis (dry powdered leaves of <i>Digitalis purpurea</i>)	1928	<i>Bull. World Hlth Org.</i> , 2 , 655, 1950	76.0	Ampoules containing ca. 2.5 g
Tubocurarine chloride (pure crystalline)	1951	<i>Bull. World Hlth Org.</i> , 2 , 65, 1949; <i>World Hlth Org. techn. Rep. Ser.</i> , 56 , 17, 1952	1.0	Ampoules containing ca. 30 mg
Arsenicals (and Antidote) and Trypanocides				
Dimercaprol (BAL)	1952	<i>World Hlth Org. techn. Rep. Ser.</i> , 68 , 18, 1953	—	Ampoules containing ca. 2 ml
Neoarsphenamine	1925	<i>Bull. World Hlth Org.</i> , 1 , 9, 1947–48	—	Ampoules containing ca. 0.3 g
Mel B	1954	<i>World Hlth Org. techn. Rep. Ser.</i> , 96 , 16, 1955	—	Ampoules containing ca. 0.1 g
MSb	1954	<i>World Hlth Org. techn. Rep. Ser.</i> , 96 , 16, 1955	—	Ampoules containing ca. 0.5 g
Oxophenarsine	1951	<i>World Hlth Org. techn. Rep. Ser.</i> , 56 , 7, 1952	—	(a) Ampoules containing ca. 60 mg or 20 mg oxophenarsine hydrochloride (b) Ampoules containing ca. 100 mg anhydrous sodium carbonate (c) Ampoules containing ca. 500 mg anhydrous sucrose
Sulpharsphenamine	1925	<i>Bull. World Hlth Org.</i> , 4 , 563, 1951; <i>World Hlth Org. techn. Rep. Ser.</i> , 56 , 17, 1952	—	Ampoules containing ca. 0.3 g
Antibiotics				
Chlortetracyclin (aureomycin) (hydrochloride)	1953	<i>Bull. World Hlth Org.</i> , 9 , 851, 1953	0.001	Ampoules containing ca. 60 mg
Bacitracin	1953	<i>Bull. World Hlth Org.</i> , 9 , 861, 1953	0.0182	Ampoules containing ca. 50 mg
Chloramphenicol (I.R.P.)	1953	<i>World Hlth Org. techn. Rep. Ser.</i> , 86 , 15, 1954	—	Ampoules containing ca. 300 mg
Dihydrostreptomycin (sulphate)	1953	<i>World Hlth Org. techn. Rep. Ser.</i> , 86 , 15, 1954; <i>Bull. World Hlth Org.</i> , 10 , 901, 1954	0.001316	Ampoules containing ca. 70 mg
Penicillin (benzylpenicillin, sodium salt)	1944	<i>Bull. Hlth Org. L. o. N.</i> , 12 , 181, 1945–46; <i>Bull. World Hlth Org.</i> , 9 , 15, 1953	0.0005988	Ampoules containing ca. 30 mg
Penicillin K (<i>n</i> -heptylpenicillin, sodium salt) (I.R.P.)	1951	<i>World Hlth Org. techn. Rep. Ser.</i> , 56 , 11, 1952; <i>Bull. World Hlth Org.</i> , 10 , 895, 1954	—	Ampoules containing ca. 20 mg
Streptomycin (sulphate)	1949	<i>World Hlth Org. techn. Rep. Ser.</i> , 2 , 11, 1950	0.001284	Ampoules containing ca. 25 mg

Physical Constants¹

General physical constants	Symbol	Value ²
Gravitational constant	<i>f</i>	= 6.670 × 10 ⁻¹¹ m ³ kg ⁻¹ s ⁻²
Cosmological gravitational constant	<i>κ</i>	= 1.865 × 10 ⁻²⁶ m kg ⁻¹ s
Normal acceleration of gravity	<i>g_n</i>	= 9.80665 m s ⁻²
Normal molar volume of an ideal gas	<i>v₀</i>	= 22.414 m ³ kmol ⁻¹ _{ch. sc.} = 22.421 m ³ kmol ⁻¹ _{ph. sc.}
Freezing point of water	<i>T₀</i>	= 273.16° K
Universal gas constant	<i>R₀</i>	= 8.3144 × 10 ³ J degree ⁻¹ kmol ⁻¹ _{ch. sc.} = 8.3167 × 10 ³ J degree ⁻¹ kmol ⁻¹ _{ph. sc.}
AVOGADRO's constant ³	<i>N_A</i>	= 6.023 × 10 ²⁶ kmol ⁻¹ _{ch. sc.} = 6.025 × 10 ²⁶ kmol ⁻¹ _{ph. sc.}
LOSCHMIDT's number ⁴	<i>n</i>	= 2.687 × 10 ¹⁹

¹) From WESTPHAL et al., *Physikalisches Wörterbuch*, 1952 (cosmic constants somewhat abbreviated and converted to MKS-units).
²) Dimensional values are expressed in the MKS- and the absolute m-s-V-A-systems (see pages 49 and 64).
³) In German-speaking countries, LOSCHMIDT's constant.
⁴) In German-speaking countries, AVOGADRO's number.

General physical constants (continued)

	Symbol	Value
FARADAY'S constant	F	$= 9.6498 \times 10^7 \text{ C kg. equiv}^{-1}_{\text{ch. sc.}}$ $= 9.6525 \times 10^7 \text{ C kg. equiv}^{-1}_{\text{ph. sc.}}$
Velocity of light in vacuum	c_0	$= 2.9979 \times 10^8 \text{ m s}^{-1}$ $c_0^2 = 8.9874 \times 10^{16} \text{ m}^2 \text{ s}^{-2}$
Absolute permittivity	ϵ_0	$= 8.8543 \times 10^{-12} \text{ F m}^{-1}$ (Dielectric constant of vacuum, electric space constant)
Absolute permeability	μ_0	$= 1.256637 \times 10^{-6} \text{ H m}^{-1} (= 4 \pi \times 10^{-7} \text{ H m}^{-1})$ (Magnetic space constant, induction constant)
Impedance of vacuum ¹	Γ_0	$= 376.727 \Omega$

Atomic constants

SMYTHE-factor ²	k_A	$= 1.000279$
Atomic weights (physical scale)		
Electron	M_e	$= 5.487 \times 10^{-4}$
Neutron	M_n	$= 1.008981$
Light hydrogen atom	M_H	$= 1.008141$
Proton	M_p	$= 1.007581$
Deuterium atom	M_D	$= 2.014732$
Deuteron	M_d	$= 2.014183$
Helium	M_{He}	$= 4.00386_0$
α -Particle	M_α	$= 4.00276_s$
Mass of a hypothetical particle of atomic weight $M \equiv 1$	m_1	$= 1.6597 \times 10^{-27} \text{ kg}$
Mass of the electron	m_0	$= 9.107 \times 10^{-31} \text{ kg}; m_1/m_0 = 1822_s$
Mass of the neutron	m_n	$= 1.675 \times 10^{-27} \text{ kg}; m_n/m_0 = 1838_s$
Mass of the light hydrogen atom	m_H	$= 1.673 \times 10^{-27} \text{ kg}; m_H/m_0 = 1837_s$
Mass of the proton	m_p	$= 1.672 \times 10^{-27} \text{ kg}; m_p/m_0 = 1836_s$
Mass of the deuterium atom	m_D	$= 3.344 \times 10^{-27} \text{ kg}; m_D/m_0 = 3671_s$
Mass of the deuteron	m_d	$= 3.343 \times 10^{-27} \text{ kg}; m_d/m_0 = 3670_s$
Mass of the helium atom	m_{He}	$= 6.645 \times 10^{-27} \text{ kg}; m_{\text{He}}/m_0 = 7296_9$
Mass of the α -particle	m_α	$= 6.643 \times 10^{-27} \text{ kg}; m_\alpha/m_0 = 7294_9$
Energy equivalents of a mass at rest		
Hypothetical particle of atomic weight $M \equiv 1$	$m_1 c_0^2$	$= 1.4917 \times 10^{-10} \text{ J} \triangleq 9.311 \times 10^2 \text{ MeV}$
Electron	$m_0 c_0^2$	$= 8.18_s \times 10^{-14} \text{ J} \triangleq 5.109 \times 10^{-1} \text{ MeV}$
Neutron	$m_n c_0^2$	$= 1.5050 \times 10^{-10} \text{ J} \triangleq 9.39 \times 10^2 \text{ MeV}$
Proton	$m_p c_0^2$	$= 1.5030 \times 10^{-10} \text{ J} \triangleq 9.38 \times 10^2 \text{ MeV}$
Deuteron	$m_d c_0^2$	$= 3.0044 \times 10^{-10} \text{ J} \triangleq 1.875 \times 10^3 \text{ MeV}$
α -Particle	$m_\alpha c_0^2$	$= 5.9707 \times 10^{-10} \text{ J} \triangleq 3.727 \times 10^3 \text{ MeV}$
Specific charge of the electron	e/m_0	$= 1.759 \times 10^{11} \text{ C kg}^{-1}$
Specific charge of the proton	e/m_p	$= 9.5797 \times 10^7 \text{ C kg}^{-1}$
Specific charge of the deuteron	e/m_d	$= 4.7922 \times 10^7 \text{ C kg}^{-1}$
Specific charge of the α -particle	$2e/m_\alpha$	$= 4.8229 \times 10^7 \text{ C kg}^{-1}$
Elementary length ³ (from FINKELNBURG)	l'	$= 1.321 \times 10^{-15} \text{ m}$
Elementary time ⁴	τ	$= 4.408 \times 10^{-24} \text{ s}$
Elementary charge	e	$= 1.602 \times 10^{-19} \text{ C}$
PLANCK'S quantum	h	$= 6.625 \times 10^{-34} \text{ J s}$ $h/e = 4.135 \times 10^{-15} \text{ Wb}$

¹⁾ $\Gamma_0 = \mu_0 c_0$.

²⁾ The SMYTHE-factor is the ratio between atomic weights on the physical and on the chemical scales. The chemical scale of atomic weights is based upon the oxygen of "natural" air (mixture of isotopes ca. 99.76% ¹⁶O + 0.04% ¹⁷O + 0.2% ¹⁸O), the atomic weight of which is arbitrarily fixed at 16.000. The physical scale of atomic weight is based upon the oxygen isotope ¹⁶O, the atomic weight of which is arbitrarily fixed at 16.0000. The ratio physical scale/chemical scale is therefore 16.00446₆:16.000 (THODE, 1947, NIER, 1950). The isotopic composition of atmospheric oxygen corresponds approximately to that of oxygen derived from limestone. Oxygen liberated from water and iron ores contains approximately 4% more ¹⁸O; the SMYTHE-factor would here be 1.000269. The average composition of "natural" oxygen therefore varies so much that the chemical scale of atomic weights is useless for the expression of atomic weights with extreme accuracy.

³⁾ COMPTON'S wave-length of the proton at rest.

⁴⁾ $\tau = l'/c_0$.

Atomic constants (continued)

	Symbol	Value
BOLTZMANN's constant	k	$= 1.380 \times 10^{-23} \text{ J degree}^{-1}$
BOHR's unit of angular momentum	$\hbar = h/2\pi$	$= 1.054 \times 10^{-34} \text{ J s}$
	$\hbar/4\pi$	$= 8.390 \times 10^{-36} \text{ J s}$
	$\hbar^2/2$	$= 5.558 \times 10^{-69} \text{ J}^2 \text{ s}^2$
	$\hbar/4\pi c_0$	$= 2.799 \times 10^{-44} \text{ J s}^2 \text{ m}^{-1}$
BOHR's magneton	μ_B	$= 1.165 \times 10^{-29} \text{ Wb m}$
Nuclear magneton	μ_K	$= 6.346 \times 10^{-33} \text{ Wb m}$
BOHR's radius of the hydrogen atom	a_0	$= 5.292 \times 10^{-11} \text{ m}$
Radius of the electron	r_0	$= 2.818 \times 10^{-15} \text{ m}$
COMPTON's wave-length of the electron	$\Delta\lambda_c$	$= 2.426 \times 10^{-12} \text{ m}$
RYDBERG constant	R_∞	$= 10,973,731 \text{ m}^{-1}$
SOMMERFELD's fine-structure constant	$1/a$	$= 137.03$
First radiation constant ...	} PLANCK's radiation constants	$c_1 = 5.954 \times 10^{-17} \text{ W m}^2$
Second radiation constant .		$c_2 = 1.438_8 \times 10^{-2} \text{ m degree}$
WIEN's displacement constant	A	$= 2.898 \times 10^{-3} \text{ m degree}$
STEFAN-BOLTZMANN constant	σ	$= 5.662 \times 10^{-8} \text{ W m}^{-2} \text{ degree}^{-4}$
CURIE constant	C	$= 1.975 \times 10^{-12} \text{ g}^2 \text{ J (J+1) H m}^2 \text{ degree}$
Dispersion constant	D	$= 26.87 \text{ m}^3 \text{ s}^{-2}$
X-ray scattering constants		
Scatter cross-section of the electron	σ	$= 6.65 \times 10^{-29} \text{ m}^2$
Constant of the mass absorption coefficient	K	$= 4.01 \times 10^{-2} \text{ m}^2 \text{ kg}^{-1}$

Cosmic constants

Solar system

Sun

Average distance from the earth	$149.5 \times 10^9 \text{ m} = 498.7 \text{ light seconds}$
Radius	$6.96 \times 10^8 \text{ m} = 109.05 \text{ times the radius of the earth}$
Mass	$1.983 \times 10^{30} \text{ kg} = 331,940 \text{ times the mass of the earth}$
Average density	$1.41 \times 10^3 \text{ kg m}^{-3}$
Acceleration of gravity at the surface	$2.74 \times 10^3 \text{ m s}^{-2}$
Total radiation	$3.72 \times 10^{26} \text{ W}$
Effective temperature	5714° K
Luminous intensity	$2.8 \times 10^{27} \text{ cd}$
Solar parallax π_\odot	$8.790''$

Earth

Radius at the equator	$6.378 \times 10^6 \text{ m}$
Polar radius	$6.356 \times 10^6 \text{ m}$
Mass	$5.977 \times 10^{24} \text{ kg}$
Average density	$5.517 \times 10^3 \text{ kg m}^{-3}$
Density of the crust	$2.60 \times 10^3 \text{ kg m}^{-3}$
Tropical year	$365^{\text{d}}24219879-0^{\text{d}}0000000614 \text{ (t}^1\text{—1900)}$
Sidereal year	$365^{\text{d}}25636042-0^{\text{d}}0000000011 \text{ (t}^1\text{—1900)}$
Mean solar day	$24^{\text{h}}3^{\text{m}}56^{\text{s}}.555 \text{ sidereal time}$
Sidereal day	$23^{\text{h}}56^{\text{m}}4^{\text{s}}.091 \text{ mean solar time}$

Moon

Average distance from the earth	$3.844 \times 10^8 \text{ m} = 60.27 \text{ times the radius of the earth}$
Radius	$1.738 \times 10^6 \text{ m} = 0.272 \text{ times the radius of the earth}$
Mass	$7.35 \times 10^{22} \text{ kg} = 0.0123 \text{ times the mass of the earth}$
Average density	$3.342 \times 10^3 \text{ kg m}^{-3}$
Sidereal period of revolution	$27^{\text{d}}321661$
Synodic period of revolution	$29^{\text{d}}530588$

¹) = current year.

Cosmic constants (Solar system, continued)

Planets	Sidereal period of revolution	Average distance from the sun (earth = 1)	Diameter m	Mass (earth = 1)	Average density kg m ⁻³	Period of rotation
Mercury	0 ^a 87 ^d 97	0.387099	4.8000 × 10 ⁶	0.055	5.72 × 10 ³	88 ^d (?)
Venus	0 224.70	0.723332	1.2200 × 10 ⁷	0.814	5.12 × 10 ³	225 ^d (?)
Earth	1 0.01	—	1.2757 × 10 ⁷	—	5.51 × 10 ³	23 ^h 56 ^m 4 ^s
Mars	1 321.74	1.523688	6.8000 × 10 ⁶	0.107	3.90 × 10 ³	24 ^h 37 ^m 23 ^s
Jupiter	11 314.92	5.202561	1.4270 × 10 ⁸	316.9	1.25 × 10 ³	9 ^h 50 ^m
Saturn	29 167.21	9.554747	1.2080 × 10 ⁸	94.8	6.1 × 10 ²	10 ^h 14 ^m
Uranus	84 8.11	19.21814	4.9700 × 10 ⁷	14.51	1.35 × 10 ³	11 ^h
Neptune	164 281.6	30.10957	5.3000 × 10 ⁷	17.19	1.32 × 10 ³	?
Pluto	248 157	39.51774	~1.0000 × 10 ⁷	~0.9	~1 × 10 ³	?

Galactic system (Milky Way)

1 light year (ly.)	9.4605 × 10 ¹⁵ m
1 parsec (pc)	3.087 × 10 ¹⁶ m = 3.263 ly.
Diameter in the plane of the Milky Way	30,000 pc
Diameter perpendicular to the plane of the Milky Way	5000 pc
Diameter of the outer layer (globular clusters, variable stars)	50,000 pc
Distance of the sun from the centre	10,000 pc
Period of rotation at the position of the sun	2 × 10 ⁸ a
Total mass of the system	5 × 10 ⁴¹ kg
Average density of the Milky Way	10 ⁻²⁰ kg m ⁻³

The Periodic System of the Elements

after LANDOLT-BÖRNSTEIN, 1950, completed from *Handbook of Chemistry and Physics*, Cleveland, 1954–55, and WESTPHAL et al., *Physikalisches Wörterbuch*, 1952

(Atomic weights 1954)

(Numbers in parentheses indicate atomic weight of most stable known isotope)

	I a b	II a b	III a b	IV a b	V a b	VI a b	VII a b	VIII a b						
1	1. H 1.0080			0. <i>n</i> 1.00896	<i>e</i> 5.485 × 10 ⁻⁴			2. He 4.003						
2	3. Li 6.940	4. Be 9.013	5. B 10.82	6. C 12.011	7. N 14.008	8. O 16.000	9. F 19.00	10. Ne 20.183						
3	11. Na 22.991	12. Mg 24.32	13. Al 26.98	14. Si 28.09	15. P 30.975	16. S** 32.066	17. Cl 35.457	18. A 39.944						
4 (3d)	19. K 39.100	20. Ca 40.08	21. Sc 44.96	22. Ti 47.90	23. V 50.95	24. Cr 52.01	25. Mn 54.94	26. Fe, 27. Co, 28. Ni 55.85 58.94 58.69						
	29. Cu 63.54	30. Zn 65.38	31. Ga 69.72	32. Ge 72.60	33. As 74.91	34. Se 78.96	35. Br 79.916	36. Kr 83.8						
5 (4d)	37. Rb 85.48	38. Sr 87.63	39. Y 88.92	40. Zr 91.22	41. Nb 92.91	42. Mo 95.95	43. Tc (99)	44. Ru, 45. Rh, 46. Pd 101.1 102.91 106.7						
	47. Ag 107.880	48. Cd 112.41	49. In 114.76	50. Sn 118.70	51. Sb 121.76	52. Te 127.61	53. I 126.91	54. Xe 131.3						
6 (5d) (4f)	55. Cs 132.91	56. Ba 137.36	57. La 138.92	72. Hf 178.6	73. Ta 180.95	74. W 183.92	75. Re 186.31	76. Os, 77. Ir, 78. Pt 190.2 192.2 195.23						
	79. Au 197.0	80. Hg 200.61	81. Tl 204.39	82. Pb 207.21	83. Bi 209.00	84. Po 210*	85. At 211	86. Rn 222.04						
7 (6d) (5f)	87. Fr 223	88. Ra 226.05	89. Ac 227 05*											
Lanthanides (rare-earth elements)														
4f	58. Ce 140.13	59. Pr 140.92	60. Nd 144.27	61. Pm (145)	62. Sm 150.43	63. Eu 152.0	64. Gd 156.9	65. Tb 158.93	66. Dy 162.46	67. Ho 164.94	68. Er 167.2	69. Tm 168.94	70. Yb 173.04	71. Lu 174.99
Actinides														
5f	90. Th 232.05	91. Pa 231.0	92. U 238.07	93. Np (237)	94. Pu (239)	95. Am (241)	96. Cm (242)	97. Bk (243)	98. Cf (244)	99. E ?	100. Fm ?	101. Mv ?		

* Calculated from the isotopic constitution, not determined analytically.
** Because of natural variations in the relative abundances of the isotopes of sulphur the atomic weight of this element has a range of ± 0.003.

Symbol	Atomic number	Name	Symbol	Atomic number	Name	Symbol	Atomic number	Name
A	18	Argon	H	1	Hydrogen	Ra	88	Radium
Ac	89	Actinium	He	2	Helium	Rb	37	Rubidium
Ag	47	Silver	Hf	72	Hafnium	Re	75	Rhenium
Al	13	Aluminium	Hg	80	Mercury	Rh	45	Rhodium
Am	95	Americium	Ho	67	Holmium	Rn	86	Radon (Niton)
As	33	Arsenic	I	53	Iodine	Ru	44	Ruthenium
At	85	Astatine	In	49	Indium	S	16	Sulphur
Au	79	Gold	Ir	77	Iridium	Sb	51	Antimony
B	5	Boron	K	19	Potassium	Sc	21	Scandium
Ba	56	Barium	Kr	36	Krypton	Se	34	Selenium
Be (Gl)	4	Beryllium	La	57	Lanthanum	Si	14	Silicon
Bi	83	Bismuth	Li	3	Lithium	Sm	62	Samarium
Bk	97	Berkelium	Lu	71	Lutecium	Sn	50	Tin
Br	35	Bromine	Mg	12	Magnesium	Sr	38	Strontium
C	6	Carbon	Mn	25	Manganese	Ta	73	Tantalum
Ca	20	Calcium	Mo	42	Molybdenum	Tb	65	Terbium
Cb	See Nb		Mv	101	Mendelevium	Tc	43	Technetium
Cd	48	Cadmium	N	7	Nitrogen	Te	52	Tellurium
Ce	58	Cerium	Na	11	Sodium	Th	90	Thorium
Cf	98	Californium	Nb (Cb)	41	Niobium (Columbium)	Ti	22	Titanium
Cl	17	Chlorine	Nd	60	Neodymium	Tl	81	Thallium
Cm	96	Curium	Ne	10	Neon	Tm	69	Thulium
Co	27	Cobalt	Ni	28	Nickel	Tu	See W	
Cr	24	Chromium	Np	93	Neptunium	U	92	Uranium
Cs	55	Caesium	O	8	Oxygen	V	23	Vanadium
Cu	29	Copper	Os	76	Osmium	W (Tu)	74	Tungsten
Dy	66	Dysprosium	P	15	Phosphorus	Xe	54	Xenon
E	99	Einsteinium	Pa	91	Protoactinium	Y	39	Yttrium
Er	68	Erbium	Pb	82	Lead	Yb	70	Ytterbium
Eu	63	Europium	Pd	46	Palladium	Zn	30	Zinc
F	9	Fluorine	Pm	61	Promethium	Zr	40	Zirconium
Fe	26	Iron	Po	84	Polonium			
Fm	100	Fermium	Pr	59	Praseodymium			
Fr	87	Francium	Pt	78	Platinum			
Ga	31	Gallium	Pu	94	Plutonium			
Gd	64	Gadolinium						
Ge	32	Germanium						
Gl	See Be							

Name	Atomic number	Symbol	Name	Atomic number	Symbol	Name	Atomic number	Symbol
Actinium	89	Ac	Hafnium	72	Hf	Radium	88	Ra
Aluminium	13	Al	Helium	2	He	Radon (Niton)	86	Rn
Americium	95	Am	Holmium	67	Ho	Rhenium	75	Re
Antimony	51	Sb	Hydrogen	1	H	Rhodium	45	Rh
Argon	18	A				Rubidium	37	Rb
Arsenic	33	As	Indium	49	In	Ruthenium	44	Ru
Astatine	85	At	Iodine	53	I			
			Iridium	77	Ir			
Barium	56	Ba	Iron	26	Fe	Samarium	62	Sm
Berkelium	97	Bk				Scandium	21	Sc
Beryllium	4	Be (Gl)	Krypton	36	Kr	Selenium	34	Se
Bismuth	83	Bi				Silicon	14	Si
Boron	5	B	Lanthanum	57	La	Silver	47	Ag
Bromine	35	Br	Lead	82	Pb	Sodium	11	Na
			Lithium	3	Li	Strontium	38	Sr
Cadmium	48	Cd	Lutecium	71	Lu	Sulphur	16	S
Caesium	55	Cs						
Calcium	20	Ca	Magnesium	12	Mg	Tantalum	73	Ta
Californium	98	Cf	Manganese	25	Mn	Technetium	43	Tc
Carbon	6	C	Mendelevium	101	Mv	Tellurium	52	Te
Cassiopeium	See Lutecium		Mercury	80	Hg	Terbium	65	Tb
Cerium	58	Ce	Molybdenum	42	Mo	Thallium	81	Tl
Chlorine	17	Cl				Thorium	90	Th
Chromium	24	Cr	Neodymium	60	Nd	Thulium	69	Tm
Cobalt	27	Co	Neon	10	Ne	Tin	50	Sn
Columbium	See Niobium		Neptunium	93	Np	Titanium	22	Ti
Copper	29	Cu	Nickel	28	Ni	Tungsten	74	W
Curium	96	Cm	Niobium	41	Nb (Cb)			
			Nitrogen	7	N	Uranium	92	U
Dysprosium	66	Dy						
Einsteinium	99	E	Osmium	76	Os	Vanadium	23	V
Erbium	68	Er	Oxygen	8	O			
Europium	63	Eu				Wolfram	See Tungsten	
			Palladium	46	Pd			
Fermium	100	Fm	Phosphorus	15	P	Xenon	54	Xe
Fluorine	9	F	Platinum	78	Pt			
Francium	87	Fr	Plutonium	94	Pu	Ytterbium	70	Yb
			Polonium	84	Po	Yttrium	39	Y
Gadolinium	64	Gd	Potassium	19	K			
Gallium	31	Ga	Praseodymium	59	Pr			
Germanium	32	Ge	Promethium	61	Pm	Zinc	30	Zn
Glucinium	See Beryllium		Protoactinium	91	Pa	Zirconium	40	Zr
Gold	79	Au						

Elements Nos. 1-8
Properties - Natural Abundance - Isotopes

Atomic Number Z	Symbol	Element <div>French German Latin</div>	Atomic Weight 1954 [<div>mol. wt.</div> <div>(chem. scale)</div>]	Valency	Melting Point °C	Boiling Point °C	Density <div>Gases: g/litre at 760 mm Hg and 0°C Solids: g/ccm or specific gravity 20°/4°C, unless otherwise stated</div>	Natural Abundance			Natural Isotopes ¹					
								in the earth's crust, etc. ⁶ %	in the atmosphere (troposphere) %	in the human body %	Isotope mass number <i>A</i>	Relative abundance %	Atomic weight (physical scale)	Mode of decay ² Radiation	Energy in MeV	Half-life ³
1	H [H ₂]	Hydrogen Hydrogène Wasserstoff Hydrogenium	1.0080 [2.016]	1	-259.14	-252.7	gas 0.08988 liquid 0.0709/-252.7° solid 0.0808/-262°	0.127 0.88	0.01 vol% 0.0007%	10.0	¹ H ² H ³ H	99.9844 0.0156 — ⁴	1.00813 2.01471 3.01695	β- no γ	0.018	12.5 y
2	He	Helium Hélium Helium Helium	4.003	0	<-272.2/26 at	-268.94	gas 0.1785 liquid 0.147/-270.8°	4.2 × 10 ⁻⁷	0.0005 vol% 0.000065%	0	³ He ⁴ He	~1.34 × 10 ⁻⁴ (atmosph.) ~100	3.01693 4.00388			
3	Li	Lithium Lithium Lithium Lithium	6.940	1	186	1336 ± 5	solid 0.534	0.003 0.005		trace	⁶ Li ⁷ Li	7.40 92.6	6.01690 7.01818			
4	Be (Gl)	Beryllium Glucinium Beryllium Beryllium	9.013	2	1278 ±	2970 (at 760 mm Hg)	solid 1.85	0.001 5 × 10 ⁻⁴		trace	⁹ Be ¹⁰ Be	100	9.01506 10.01675	β- no γ	0.56	2.7 × 10 ⁶ y
5	B	Boron Bore Bor Boron or Borium	10.82	3	2300	~2550 (subl.)	crystalline 2.54 amorphous 2.45	5 × 10 ⁻⁴ 0.0014		trace	¹⁰ B ¹¹ B	18.83 81.17	10.01618 11.01284			
6	C	Carbon Carbone Kohlenstoff Carboneum	12.011	2, 4	amorphous, graphite: (subl.) 3652-97; diamond > 3500	All three forms: 4200 (?)	amorphous 1.8-2.1 graphite 2.25 diamond 3.51	0.027 0.087	CO ₂ : 0.03 vol% 0.03-0.04%	18.0	¹² C ¹³ C ¹⁴ C	98.892 1.108	12.00386 13.00756 14.00770	β- no γ	0.155	5700 y
7	N [N ₂]	Nitrogen Azote Stickstoff Nitrogenium	14.008 [28.016]	3, 5	-209.86	-195.8	gas 1.25060 liquid 0.808/-195.8° solid 1.026/-252.5°	<0.001 0.03	78.06 vol% 75.31 %	3.0	¹⁴ N ¹⁵ N	99.64 0.36	14.00754 15.00489			
8	O [O ₂]	Oxygen Oxygen Oxygène Sauerstoff Oxygenium	16.000 [32.000]	2	-218.4	-183.0	gas 1.4290 liquid 1.14/-183° solid 1.426/-252.5°	46.43 49.4	20.99 vol% 22.95 %	65.0	¹⁶ O ¹⁷ O ¹⁸ O	99.76 0.04 0.20	16.00000 (standard) 17.00450 18.0049			

Elements Nos. 9-17
Properties – Natural Abundance – Isotopes

85

9	F [F ₂]	Fluorine Fluor Fluor Fluor	19.00 [38.00]	1	-223	-188	gas 1.69/15° liquid 1.108/-187° solid 1.3/-223°	0.077 0.027	~0.009	¹⁹ F	100	19.00454
10	Ne	Neon Néon Neon Neon	20.183	0	-248.67	-245.9	gas 0.90020 liquid 1.204/-245.9° solid (1.0)	5 × 10 ⁻⁷	0 0.0018 vol% 0.0014 %	²⁰ Ne ²¹ Ne ²² Ne	90.51 0.28 9.21	19.99872 20.99963 21.99844
11	Na	Sodium Sodium Natrium Natrium	22.991	1	97.5	880	liquid 0.973/97.5° solid 0.971	2.85 2.64	0.109	²³ Na	100	22.99618
12	Mg	Magnesium Magnésium Magnesium Magnesium	24.32	2	651	1110	liquid 1.57/650° solid 1.74/5°	2.09 1.94	0.036	²⁴ Mg ²⁶ Mg ²⁸ Mg	78.6 10.1 11.3	23.9924 24.9938 25.9898
13	Al	Aluminium (Aluminium) Aluminium Aluminium Aluminium	26.98	3	659.7	2450	liquid 2.4/658° solid 2.702	8.13 7.51	~0.001	²⁷ Al	100	
14	Si	Silicon Silicium Silizium Silicium	28.09	4	adamantine: 1420	2600	adamantine: 2.42 amorphous: 2.0 graphitoidal: ca. 2.4	27.77 25.75	~0.002	²⁸ Si ²⁹ Si ³⁰ Si	92.28 4.67 3.05	27.9866 28.9866 29.9832
15	P [P ₄]	Phosphorus Phosphore Phosphor Phosphorus	30.975 [123.900]	3, 5	yellow: 44.1 (ignites at 34°) red: 590 (at 43 at)	280	yellow: solid 1.82 red: liquid 1.75/44.5° red: solid 2.20 violet: solid 2.36 black: 2.7	0.130 0.12	1.16	³¹ P	100	30.9843
16	S [S ₈]	Sulphur (Sulfur) Soufre Schwefel Sulphur	32.066 ⁵ [256.53]	2, 4, 6	rhomb.: 112.8 monocl.: 119.0	444.6	liquid 1.803/115° rhomb.: solid 2.07 monocl.: solid 1.957	0.052 0.048	0.196	³² S ³³ S ³⁴ S ³⁶ S	95.06 0.74 4.18 0.0136	31.98085 32.9800 33.97710 35.978
17	Cl [Cl ₂]	Chlorine Chlore Chlor Chlorum or Chlorinum	35.457 [70.914]	1, 3, 5, 7	-103 ± 5	- 34.6	gas 3.214 liquid 1.776/-34.6° solid (1.9)	0.055 0.19	0.156	³⁵ Cl ³⁷ Cl	75.4 24.6	34.97867 36.97750

¹⁾ From BRADFORD, J. R., in *Handbook of Chemistry and Physics*, Cleveland, 1954-55, pages 394-447.

²⁾ α = alpha particle (helium nucleus = 2 protons + 2 neutrons), β⁻ = beta particle (negative electron), β⁺ = positron, γ = gamma ray, e⁻ = internal electron conversion, K = orbital electron capture, IT = isomeric transition.

³⁾ y = year, d = day, h = hour, m = minute, s = second.

⁴⁾ The numbers of ¹H and ³H atoms are approximately in the ratio 10¹⁷:1.

⁵⁾ Because of natural variations in the relative abundances of the isotopes of sulphur the atomic weight of this element has a range of ± 0.003.

⁶⁾ Values in roman type apply to the earth's crust only; values in *italics* are total percentages in the lithosphere (outer 10 miles), hydrosphere and atmosphere (after REMY, H., *Lehrbuch der Anorganischen Chemie*, 7th edition, Leipzig, 1954).

Elements Nos. 18–26
Properties – Natural Abundance – Isotopes

Atomic Number <i>Z</i>	Symbol	Element <div>French German Latin</div>	Atomic Weight 1954 [<div>or mol. wt.] (chem. scale)</div>	Valen- len- cy	Melting Point °C	Boiling Point °C	Density <div>Gases: g/litre at 760 mm Hg and 0°C Solids: g/ccm or specific gravity 20°/4°C, unless otherwise stated</div>	Natural Abundance			Natural Isotopes ¹					
								in the earth's crust, etc. ⁴ %	in the atmosphere (troposphere) %	in the human body %	Isotope mass number <i>A</i>	Relative abun- dance %	Atomic weight (physical scale)	Mode of decay ² Radi- ation	Energy in MeV	Half- life ³
18	A	Argon <div>Argon Argon Argon</div>	39.944	0	−189.2	−185.7	gas 1.784 liquid 1.40/−186° solid 1.65/−233°	3.6×10^{-4}	0.9323 vol% 1.292%	0	³⁶ A ³⁸ A ⁴⁰ A	0.34 0.06 99.6	35.9780 37.974 39.9756			
19	K	Potassium <div>Potassium Kalium Kalium</div>	39.100	1	62.3	760	liquid 0.83/62° solid 0.86	2.60 2.40		0.265	³⁹ K ⁴⁰ K	93.1 0.0119	39.9773	β^- β^+ γ (K)	1.4 1.5	$\sim 1.4 \times 10^9$ y
20	Ca	Calcium <div>Calcium Kalzium Calcium</div>	40.08	2	842–848	1240	solid 1.55	3.63 3.39		2.01	⁴¹ K ⁴⁰ Ca ⁴² Ca ⁴³ Ca ⁴⁴ Ca ⁴⁶ Ca ⁴⁸ Ca	6.9 96.92 0.64 0.13 2.13 0.0032 0.179	40.9747 39.9753 41.9711 42.9723			
21	Sc	Scandium <div>Scandium Scandium Scandium</div>	44.96	3	1200	2400	solid 3.02/10°	6×10^{-4}		0	⁴⁵ Sc	100	44.9669			
22	Ti	Titanium <div>Titane Titan Titanium</div>	47.90	2, 3, 4	1800	(>3000)	solid 4.50	0.629 0.58		0	⁴⁶ Ti ⁴⁷ Ti ⁴⁸ Ti ⁴⁹ Ti ⁵⁰ Ti	7.95 7.75 73.45 5.51 5.34	45.9661 46.9647 47.9631 48.9646 49.9621			
23	V	Vanadium <div>Vanadium Vanadium Vanadium</div>	50.95	2, 3, 4, 5	1710	(3000)	solid 5.96	0.021 0.016		0	⁵⁰ V ⁵¹ V	0.25 99.75	50.9577			
24	Cr	Chromium <div>Chrome Chrom Chromium</div>	52.01	2, 3, 6	(1920)	(2327)	solid 7.1	0.037 0.033		0	⁵⁰ Cr ⁵² Cr ⁵³ Cr ⁵⁴ Cr	4.41 83.46 9.54 2.61	49.96436 51.95590 52.95519 53.95419			
25	Mn	Manganese <div>Manganèse Mangan Manganum(-ium) or Manganesium</div>	54.94	2, 3, 4, 6, 7	(1260)	(1900)	solid 7.20	0.096 0.085		~ 0.001	⁵⁵ Mn	100	54.957			
26	Fe	Iron <div>Fer Eisen Ferrum</div>	55.85	2, 3, 6	1528	(2730)	liquid 6.9/1530° solid 7.85–7.88	5.12 4.7		0.010	⁵⁴ Fe ⁵⁶ Fe ⁵⁷ Fe ⁵⁸ Fe	5.90 91.52 2.245 0.33	53.95766 55.95332 56.95477 57.95083			

Elements Nos. 27–35
Properties – Natural Abundance – Isotopes

27	Co	Cobalt	58.94	2, 3	1495	(2900)	solid	8.9	0.001 0.0018	~0.001	⁵⁹ Co	100
		Cobalt Kobalt Cobaltum										
28	Ni	Nickel	58.69	2, 3	1455	(2900)	solid	8.90	0.019 0.018	~0.001	⁵⁸ Ni ⁶⁰ Ni ⁶¹ Ni ⁶² Ni ⁶⁴ Ni	67.8 26.2 1.2 3.7 1.1 59.94981 60.9540 61.94959 63.94744
		Nickel Niccolum										
29	Cu	Copper	63.54	1, 2	1083	2336	liquid solid	8.3/1083° 8.93–8.95	0.002 0.010	~0.002	⁶³ Cu ⁶⁵ Cu	69.09 30.91 64.955
		Cuivre Kupfer Cuprum										
30	Zn	Zinc	65.38	2	419.17	907	liquid solid	6.7/463° 7.133	0.02	~0.002	⁶⁴ Zn ⁶⁶ Zn ⁶⁷ Zn ⁶⁸ Zn ⁷⁰ Zn	48.87 27.62 4.12 18.71 0.69 63.95356 65.94667 66.9482 67.9488 69.9460
		Zinc Zink Zincum										
31	Ga	Gallium	69.72	2, 3	29.92	1983	liquid solid	6.095/29.8° 5.904/29.6°	5×10 ⁻⁴	0	⁶⁹ Ga ⁷¹ Ga	60.0 40.0 68.956 70.954
		Gallium Gallium Gallium										
32	Ge	Germanium	72.60	4	958.5	(2700)	solid	5.35	1×10 ⁻⁴	0	⁷⁰ Ge ⁷² Ge ⁷³ Ge ⁷⁴ Ge ⁷⁶ Ge	20.45 27.41 7.77 36.58 7.79
		Germanium Germanium Germanium										
33	As	Arsenic	74.91 [299.64]	3, 5	crystalline: 814/36 at yellow: 358	(subl.) 615	black: cryst. amorphous 3.7 yellow: solid 2.0	5.727/14°	5.5×10 ⁻⁴	0	⁷⁵ As	100
		Arsenic Arsen Arsenicum										
34	Se	Selenium	78.96 [631.68]	2, 4, 6	grey: 217 red: 170–180	grey and red: 688	grey: solid red: monocl.	4.79/15° 4.46/25°	8×10 ⁻⁵	0	⁷⁴ Se ⁷⁶ Se ⁷⁷ Se ⁷⁸ Se ⁸⁰ Se ⁸² Se	0.96 9.12 7.50 23.61 49.96 8.84
		Selenium Selen Selenium										stable
35	Br	Bromine	79.916 [159.832]	1, 3, 5, 7	-7.2	58.78	gas liquid solid	7.59 3.119 (3.4)	6×10 ⁻⁴	~0.002	⁷⁹ Br ⁸¹ Br	50.57 49.43 79.9440
		Bromine Brom Bromum(-ium) or Brominium										

1) From BRADFORD, J. R., in *Handbook of Chemistry and Physics*, Cleveland, 1954–55, pages 394–447.

2) α = alpha particle (helium nucleus = 2 protons + 2 neutrons), β^- = beta particle (negative electron), β^+ = positron, γ = gamma ray, e^- = internal electron conversion, K = orbital electron capture, IT = isomeric transition.

3) y = year, d = day, h = hour, m = minute, s = second.

4) Values in roman type apply to the earth's crust only; values in *italics* are total percentages in the lithosphere (outer 10 miles), hydrosphere and atmosphere (after REMY, H., *Lehrbuch der Anorganischen Chemie*, 7th edition, Leipzig, 1954).

Elements Nos. 36–43
Properties – Natural Abundance – Isotopes

Atomic Number <i>Z</i>	Symbol	Element <div>French German Latin</div>	Atomic Weight 1954 [or mol. wt. (chem. scale)]	Valen- cy	Melting Point °C	Boiling Point °C	Density <div>Gases: g/litre at 760 mm Hg and 0°C Solids: g/ccm or specific gravity 20°/4°C, unless otherwise stated</div>	Natural Abundance			Natural Isotopes ¹						
								in the earth's crust, etc. ⁵ %	in the atmosphere (troposphere) %	in the human body %	Isotope mass number <i>A</i>	Relative abun- dance %	Atomic weight (physical scale)	Mode of decay ² Radi- ation	Energy in MeV	Half- life ³	
36	Kr	Krypton Krypton Krypton Krypton	83.8	0	−156.6	−152.9	gas 3.708 liquid 2.155/−152.9°	1.9×10^{-8}	0.0001 vol% 0.0003%	0	⁷⁸ Kr ⁸⁰ Kr ⁸² Kr ⁸³ Kr(⁴) ⁸⁴ Kr ⁸⁶ Kr	0.354 2.27 11.56 11.55 56.90 17.37	77.945 81.938 83.939 85.939				stable
37	Rb	Rubidium Rubidium Rubidium Rubidium	85.48	1	38.5	700	liquid 1.475/38.5° solid 1,532	3×10^{-4} 0.0034		0	⁸⁵ Rb ⁸⁷ Rb	72.15 27.85			β^- γ (?)	0.275	6×10^{10} y
38	Sr	Strontium Strontium Strontium Strontium	87.63	2	757 (800)	1150 (1364)	solid 2.6	0.018 0.017		0	⁸⁴ Sr ⁸⁶ Sr ⁸⁷ Sr ⁸⁸ Sr	0.55 9.75 6.96 82.74					stable
39	Y	Yttrium Yttrium Yttrium Yttrium	88.92	3	1490	(2500)	solid 5.51	0.005		0	⁸⁹ Y	100					stable
40	Zr	Zirconium Zirconium Zirkon Zirkonium	91.22	4	1860	> 2900	solid 6.4	0.023		0	⁹⁰ Zr ⁹¹ Zr ⁹² Zr ⁹⁴ Zr ⁹⁶ Zr	51.46 11.23 17.11 17.40 2.8					stable
41	Nb (Cb)	Niobium (Columbium) (Columbium) Niob (Columbium) Niobium	92.91	3, 5	2415 (ignites at 1950°)	~3700	solid 8.55	4×10^{-5}		0	⁹³ Nb	100					stable
42	Mo	Molybdenum Molybdène Molybdän Molybdaenum	95.95	2, 3, 4, 5, 6	2620 ± 10 (4800?)	3700 (4800?)	solid 10.2	7.2×10^{-4}		trace	⁹² Mo ⁹⁴ Mo ⁹⁵ Mo ⁹⁶ Mo ⁹⁷ Mo ⁹⁸ Mo ¹⁰⁰ Mo	15.05 9.35 15.78 16.56 9.60 24.60 9.68	94.945 95.946 96.945 97.994 99.939				
43	Tc	Technetium Technétium Technetium Technetium	(99)	4, 6, 7	—	—	—	—		—	^{92–102} Tc and ¹⁰⁶ Tc	All very unstable, except ⁹⁷ Tc (half-life about 10 ³ y) and ⁹⁹ Tc (half-life 5 × 10 ⁶ y); no natural isotopes					

Elements Nos. 44–51
Properties – Natural Abundance – Isotopes

44	Ru	Ruthenium Ruthenium Ruthenium Ruthenium	101.1	3, 4, 6, 8	hex. 2450	hex. 4150	hexagonal 12.063	5×10^{-6}	0	⁹⁶ Ru ⁹⁸ Ru ⁹⁹ Ru ¹⁰⁰ Ru ¹⁰¹ Ru ¹⁰² Ru ¹⁰⁴ Ru	5.68 2.22 12.81 12.70 16.98 31.34 18.27	95.945 98.944	
45	Rh	Rhodium Rhodium Rhodium Rhodium	102.91	1, 2, 3, 4	1985	(>2500)	solid 12.5	1×10^{-6}	0	¹⁰³ Rh	100		stable
46	Pd	Palladium Palladium Palladium Palladium	106.7	2, 4	1549.4	ca. 2540	liquid 11/1550° solid 11.97	5×10^{-6}	0	¹⁰² Pd ¹⁰⁴ Pd ¹⁰⁵ Pd ¹⁰⁶ Pd ¹⁰⁸ Pd ¹¹⁰ Pd	0.8 9.3 22.6 27.1 26.7 13.5	105.946 109.944	
47	Ag	Silver Argent Silber Argentum	107.880	1	960.8	1950 (2170?)	liquid 9.4/960° solid 10.5	4×10^{-6}	0	¹⁰⁷ Ag ¹⁰⁸ Ag	51.35 48.65	106.950 108.949	stable stable
48	Cd	Cadmium Cadmium Kadmium Cadmium	112.41	2	320.9	767 ± 2	liquid 8.0/320° solid 8.642	1.1×10^{-5}	0	¹⁰⁶ Cd ¹⁰⁸ Cd ¹¹⁰ Cd ¹¹¹ Cd ¹¹² Cd ¹¹³ Cd ¹¹⁴ Cd ¹¹⁶ Cd	1.22 0.89 12.43 12.86 23.79 12.34 28.81 7.66		stable stable
49	In	Indium Indium Indium Indium	114.76	1, 3	156.4	1450	solid 7.30	1×10^{-5}	0	¹¹³ In ¹¹⁵ In	4.16 95.84		stable 6×10^{14} y
50	Sn	Tin Etain Zinn Stannum	118.70	2, 4	231.89	2260	liquid 6.98/232° cubic (α): solid 5.750 tetr. (β ⁻): solid 7.28 rhomb. (γ ⁻): solid 6.52–6.56	6×10^{-4}	trace	¹¹² Sn ¹¹⁴ Sn ¹¹⁵ Sn ¹¹⁶ Sn ¹¹⁷ Sn ¹¹⁸ Sn ¹¹⁹ Sn ¹²⁰ Sn ¹²² Sn ¹²⁴ Sn	1.01 0.68 0.35 14.28 7.67 23.84 8.68 32.75 4.74 6.01	115.943 117.940 119.930 121.946 123.945	stable stable $> 1.7 \times 10^{17}$ y
51	Sb	Antimony Antimoine Antimon Stibium	121.76	3, 5	630.5	1380	liquid 6.55/631° solid 6.691	2.3×10^{-5}	0	¹²¹ Sb ¹²³ Sb	57.25 42.75		2 β-

1) From BRADFORD, J. R., in *Handbook of Chemistry and Physics*, Cleveland, 1954–55, pages 394–447.

2) α = alpha particle (helium nucleus = 2 protons + 2 neutrons), β⁻ = beta particle (negative electron), β⁺ = positron, γ = gamma ray, e⁻ = internal electron conversion, K = orbital electron capture, IT = isomeric transition.

3) y = year, d = day, h = hour, m = minute, s = second.

4) Fission product (thermal neutron fission of ²³⁵U).

5) Values in roman type apply to the earth's crust only; values in *italics* are total percentages in the lithosphere (outer 10 miles), hydrosphere and atmosphere (after REMY, H., *Lehrbuch der Anorganischen Chemie*, 7th edition, Leipzig, 1954).

Elements Nos. 52–58
Properties – Natural Abundance – Isotopes

Atomic Number <i>Z</i>	Symbol	Element <div>French German Latin</div>	Atomic Weight 1954 [<div>or mol. wt.] (chem. scale)</div>	Valen- cy	Melting Point °C	Boiling Point °C	Density Gases: g/litre at 760 mm Hg and 0°C Solids: g/ccm or specific gravity 20°/4°C, unless otherwise stated	Natural Abundance			Natural Isotopes ¹						
								in the earth's crust, etc. ⁵ %	in the atmosphere (troposphere) %	in the human body %	Isotope mass number <i>A</i>	Relative abun- dance %	Atomic weight (physical scale)	Mode of decay ² Radi- ation	Energy in MeV	Half- life ³	
52	Te [Te ₂]	Tellurium Tellure Tellur Tellurium	127.61 [255.22]	2, 4, 6	452	1390	rhomb.: 6.25 amorphous: 6.00	1×10 ⁻⁶		0	¹²⁰ Te ¹²² Te ¹²³ Te ¹²⁴ Te ¹²⁵ Te ¹²⁶ Te ¹²⁸ Te ¹³⁰ Te	0.090 2.47 0.89 4.74 7.03 18.72 31.75 34.27					stable stable
53	I [I ₂]	Iodine Iode Jod Jodium	126.91 [253.82]	1, 3, 5, 7	113.5	184.35	gas 11.27 solid 4.93	6×10 ⁻⁶		0.016	¹²⁷ I	100	126.932				
54	Xe	Xenon Xénon Xenon Xenon	131.3	0	-111.9	-107.1	gas 5.851 liquid 3.52/-109° solid 2.7/-140°	2.4×10 ⁻⁹	9×10 ⁻⁶ vol% 4×10 ⁻⁵ %	0	¹²⁴ Xe ¹²⁶ Xe ¹²⁸ Xe ¹²⁹ Xe ¹³⁰ Xe ¹³¹ Xe(⁴) ¹³² Xe ¹³⁴ Xe ¹³⁶ Xe	0.095 0.088 1.91 26.24 4.053 21.24 26.93 10.52 8.93	128.946 131.946			stable stable	
55	Cs	Caesium (Cesium) Césium Caesium Caesium	132.91	1	28.5	670	solid 1.873	7×10 ⁻⁵		0	¹³² Cs	100					
56	Ba	Barium Baryum Barium Barium	137.36	2	850	1140	solid 3.5	0.048 0.047		0	¹³⁰ Ba ¹³² Ba ¹³⁵ Ba ¹³⁶ Ba ¹³⁷ Ba ¹³⁸ Ba	0.103 0.096 6.56 7.74 11.25 71.83				stable stable	
57	La	Lanthanum Lanthane Lanthan Lanthan	138.92	3	826	1800	solid 6.15	5×10 ⁻⁴		0	¹³⁸ La	0.089		β- γ e-	1.0 1.0	1.2×10 ¹² y	
58	Ce	Cerium Cérium Zer Cerium	140.13	3, 4	640	1400	cubic: 6.90 hexagonal: 6.7	0.0015 0.0022		0	¹³⁶ Ce ¹³⁸ Ce ¹⁴⁰ Ce ¹⁴² Ce	0.195 0.265 88.45 11.10	138.955				

Elements Nos. 59-67
Properties - Natural Abundance - Isotopes

59	Pr	Praseodymium Praseodymium Praseodymium Praseodymium	140.92	3, 4, 5	940	-	solid	6.5	3.5×10^{-4}	0	¹⁴¹ Pr	100	
60	Nd	Neodymium Neodymium Neodymium Neodymium	144.27	3	840	-	solid	6.9	0.0012	0	¹⁴² Nd ¹⁴³ Nd ¹⁴⁴ Nd ¹⁴⁵ Nd ¹⁴⁶ Nd ¹⁴⁸ Nd ¹⁵⁰ Nd	27.13 12.20 23.87 8.30 17.18 5.72 5.60	145.964 147.946 149.970 >2x10 ¹⁵ y
61	Pm	Promethium Promethium Promethium Promethium	(145)	-	-	-	-	-	-		Pm ¹⁴¹⁻¹⁴³ ¹⁴⁵⁻¹⁵¹ ^{153, 156} all very unstable; no natural isotopes		
62	Sm	Samarium Samarium Samarium Samarium	150.43	2, 3	1300-1400	-	solid	7.7-7.8	5×10^{-4}	0	¹⁴⁴ Sm ¹⁴⁷ Sm ¹⁴⁸ Sm ¹⁴⁹ Sm ¹⁵⁰ Sm ¹⁵² Sm ¹⁵⁴ Sm	2.87 14.94 11.24 13.85 7.36 26.90 22.84	α, no e ⁻ 2.1 6.7x10 ¹¹ y
63	Eu	Europium Europium Europium Europium	152.0	2, 3	1150 ± 50	-	solid	5.3	1.4×10^{-4}	0	¹⁵¹ Eu ¹⁵³ Eu	47.77 52.23	
64	Gd	Gadolinium Gadolinium Gadolinium Gadolinium	156.9	3	-	-	solid	7.9	5×10^{-4}	0	¹⁵² Gd ¹⁵⁴ Gd ¹⁵⁵ Gd ¹⁵⁶ Gd ¹⁵⁷ Gd ¹⁵⁸ Gd ¹⁶⁰ Gd	0.20 2.15 14.78 20.59 15.71 24.78 21.79	154.977 155.977 156.976 157.976 159.976
65	Tb	Terbium Terbium Terbium Terbium	158.93	3	-	-	solid	8.3	7×10^{-5}	0	¹⁵⁹ Tb	100	
66	Dy	Dysprosium Dysprosium Dysprosium Dysprosium	162.46	3	-	-	solid	8.5	5×10^{-4}	0	¹⁵⁶ Dy ¹⁵⁸ Dy ¹⁶⁰ Dy ¹⁶¹ Dy ¹⁶² Dy ¹⁶³ Dy ¹⁶⁴ Dy	0.052 0.0902 2.29 18.88 25.52 24.97 28.18	
67	Ho	Holmium Holmium Holmium Holmium	164.94	3	-	-	-	-	7×10^{-5}	0	¹⁶⁵ Ho	100	

1) From BRADFORD, J. R., in *Handbook of Chemistry and Physics*, Cleveland, 1954-55, pages 394-447.

2) α = alpha particle (helium nucleus = 2 protons + 2 neutrons), β⁺ = positron, γ = gamma ray, e⁻ = internal electron conversion, K = orbital electron capture, IT = isomeric transition.

3) y = year, d = day, h = hour, m = minute, s = second.

4) Fission product (thermal neutron fission of ²³⁵U).

5) Values in roman type apply to the earth's crust only; values in *italics* are total percentages in the lithosphere (outer 10 miles), hydrosphere and atmosphere (after REMY, H., *Lehrbuch der Anorganischen Chemie*, 7th edition, Leipzig, 1954).

Elements Nos. 68–75
Properties – Natural Abundance – Isotopes

Atomic Number <i>Z</i>	Symbol	Element <div>French German Latin</div>	Atomic Weight 1954 [<div>or mol. wt.] (chem. scale)</div>	Valen- len- cy	Melting Point °C	Boiling Point °C	Density <div>Gases: g/litre at 760 mm Hg and 0°C Solids: g/ccm or specific gravity 20°/4°C, unless otherwise stated</div>	Natural Abundance			Natural Isotopes ¹					
								in the earth's crust, etc. ⁵ %	in the atmosphere (troposphere) %	in the human body %	Isotope mass number <i>A</i>	Relative abun- dance %	Atomic weight (physical scale)	Mode of decay ² Radi- ation	Energy in MeV	Half- life ³
68	Er	Erbium Erbium Erbium Erbium	167.2	3	–	–	solid 9.16	4×10^{-4}		0	¹⁶² Er ¹⁶⁴ Er ¹⁶⁶ Er ¹⁶⁷ Er ¹⁶⁸ Er ¹⁷⁰ Er	0.136 1.56 33.41 22.94 27.07 14.88				
69	Tm	Thulium Thulium Thulium Thulium	168.94	3	–	–	solid 9.3	7×10^{-5}		0	¹⁶⁹ Tm	100				
70	Yb	Ytterbium Ytterbium Ytterbium Ytterbium	173.04	3	–	–	solid 7.0	5×10^{-4}		0	¹⁶⁷ Yb ¹⁶⁸ Yb ¹⁷⁰ Yb ¹⁷¹ Yb ¹⁷² Yb ¹⁷³ Yb ¹⁷⁴ Yb ¹⁷⁶ Yb	<0.002 0.14 3.03 14.34 21.88 16.18 31.77 12.65				
71	Lu	Lutecium (Lutetium) Lutécium Lutetium (Cassiopeiium) Lutecium	174.99	3, 4	–	–	solid 9.7	1×10^{-5}		0	¹⁷⁵ Lu ¹⁷⁶ Lu	97.5 2.5		β- γ	0.4 0.27	7.2×10^{10} y
72	Hf	Hafnium Hafnium Hafnium Hafnium	178.6	4	2207 (1700)	(> 3200)	solid 13.3	0.0025		0	¹⁷⁴ Hf ¹⁷⁶ Hf ¹⁷⁷ Hf ¹⁷⁸ Hf ¹⁷⁹ Hf ¹⁸⁰ Hf	0.18 5.15 18.39 27.08 13.78 35.44				stable stable
73	Ta	Tantalum Tantale Tantal Tantalum	180.95	3, 5	3027	(ca.4100)	metallic 16.6 powder 14.491	1.2×10^{-5}		0	¹⁸¹ Ta	100				
74	W	Tungsten (Wolfram) Tungstène Wolfram Wolframium	183.92	2, 4, 5, 6	3370	5900	solid 19.3	0.0055		0	¹⁸⁰ W ¹⁸² W ¹⁸³ W ¹⁸⁴ W ¹⁸⁶ W	0.126 26.31 14.28 30.64 28.64				stable
75	Re	Rhenium Rhénium Rhenium Rhenium	186.31	4–8	3167 ± 60	–	solid 20.53	1×10^{-7}		0	¹⁸⁵ Re ¹⁸⁷ Re	37.07 62.93		β-	0.043	4×10^{12} y

⁶) Values in roman type apply to the earth's crust only; values in *italics* are total percentages in the lithosphere (outer 10 miles), hydrosphere and atmosphere (after Remy, H., *Lehrbuch der Anorganischen Chemie*, 7th edition, Leipzig, 1954).

Elements Nos. 82-84
Properties - Natural Abundance - Isotopes

Atomic Number	Symbol	Element <div>French German Latin</div>	Atomic Weight 1954 <div>[or mol. wt.] (chem. scale)</div>	Valency	Melting Point °C	Boiling Point °C	Density <div>Gases: g/litre at 760 mm Hg and 0°C Solids: g/ccm or specific gravity 20°/4°C, unless otherwise stated</div>	Natural Abundance			Natural Isotopes ¹					
								in the earth's crust, etc. ⁴ %	in the atmosphere (troposphere) %	in the human body %	Isotope mass number <i>A</i>	Relative abun- dance %	Atomic weight (physical scale)	Mode of decay ² Radi- ation	Energy in MeV	Half- life ³
82	Pb	Lead <div>Plomb Blei Plumbum</div>	207.21	2, 4	327.20	1613	solid 11.3437/16°	0.002		0	²⁰⁴ Pb	1.37	206.061			
											²⁰⁶ Pb	26.26				
											²⁰⁷ Pb	20.82				
											²⁰⁸ Pb	51.55	208.060			
											²¹⁰ Pb		RaD	β- γ	0.029/0.017 0.007...0.047	25 y
											²¹¹ Pb		AcB	β- γ	1.4/0.5 0.829	36.1 m
											²¹² Pb		ThB	β- γ	0.350/0.590 0.238/0.115/ 0.176	10.6 h
											²¹⁴ Pb		RaB	β- γ	0.250/0.300 0.72 0.053...0.351 0.584...1.438	26.8 m
83	Bi	Bismuth <div>Bismuth Wismut Bismutum (Bismuthum)</div>	209.00	3, 5	271.3	1560±5	solid 9.8	3.4×10 ⁻⁶		0	²⁰⁹ Bi	100	209.056			
											²¹⁰ Bi		RaE	α β- γ	5.0 1.080/1.165 0.08	4.85 d
														α	4.93	~10 ⁶ y
											²¹¹ Bi		AcC	α β- γ	6.618/6.272 0.35/0.46	2.16 m
											²¹² Bi		ThC	α β- γ	6.074/6.113/ 5.762/5.601 2.25	60.5 m
											²¹⁴ Bi		RaC	α β- γ	0.040...0.719 5.444/5.505 1.650/3.173 0.426...2.420	19.7 m
84	Po	Polonium <div>Polonium Polonium Polonium</div>	(210)	-	(1800)	-	-	1.5× 10 ⁻¹⁵		-	²¹⁰ Po		RaF	α γ	5.303 0.803	138 d
											²¹¹ Po		AcC'	α	7.434	0.52 s ↓ IT
											²¹² Po		ThC'	α	7.14	25 s
											²¹⁴ Po		RaC'	α	8.776/10.574	3×10 ⁻⁷ s
											²¹⁵ Po		AcA	α	7.683	1.64× 10 ⁻⁴ s
											²¹⁶ Po		ThA	α β- α β- α	7.365 6.774 5.998	1.83× 10 ⁻³ s 0.158 s 3.05 m

211	(1, 3, 5, 7)	—	—	4×10^{-23}	—	215At	α	8.04	$\sim 10^{-4}$ s
211	(1, 3, 5, 7)	—	—	—	—	218At	α β-	6.72	~ 2 s
222.04	0	-110	-61.8	4×10^{-17}	gas liquid solid (4)	219Rn	α	6.824/6.558/ 6.434/6.224 0.067/0.392	3.92 s
223	1	—	—	—	—	220Rn	γ	6.282	54.5 s
223	1	—	—	—	—	222Rn	α	5.486	3.825 d
226.05	2	960	1140	7×10^{-23}	solid (5?)	223Fr	β- γ	1.20 0.049/0.095	21 m
226.05	2	960	1140	2.4×10^{-10} 7×10^{-12}	solid (5?)	223Ra	α	5.719/5.607/ 5.533/5.439 0.144...0.340	11.2 d
227.05	—	—	—	3×10^{-15}	—	224Ra	γ	5.66/5.448/ 5.194 0.250	3.64 d
227.05	—	—	—	—	—	226Ra	α	4.795/4.611/ 4.21	1620 y
227.05	—	—	—	—	—	228Ra	γ	0.188	—
227.05	—	—	—	—	—	228Ra	β-	0.030	6.7 y
227.05	—	—	—	—	—	227Ac	α β- γ	4.94 0.02 0.037	27.7 y
227.05	—	—	—	—	—	228Ac	α β- γ	4.54 1.5/2.0 0.058...0.969	6.13 h

1) From BRADFORD, J. R., in *Handbook of Chemistry and Physics*, Cleveland, 1954–55, pages 394–447.
2) α = alpha particle (helium nucleus = 2 protons + 2 neutrons), β⁺ = positron, γ = gamma ray, e⁻ = internal electron conversion, K = orbital electron capture, IT = isomeric transition.
3) y = year, d = day, h = hour, m = minute, s = second.
4) Values in roman type apply to the earth's crust only; values in *italic* are total percentages in the lithosphere (outer 10 miles), hydrosphere and atmosphere (after REMY, H., *Lehrbuch der Anorganischen Chemie*, 7th edition, Leipzig, 1954).

Elements Nos. 90–92
Properties – Natural Abundance – Isotopes

Atomic Number	Symbol	Element <div>French German Latin</div>	Atomic Weight 1954 [<div>mol. wt. (chem. scale)</div>]	Valency	Melting Point °C	Boiling Point °C	Density <div>Gases: g/litre at 760 mm Hg and 0°C Solids: g/ccm or specific gravity 20°/4°C, unless otherwise stated</div>	Natural Abundance			Natural Isotopes ¹					
								in the earth's crust, etc. ⁴ %	in the atmosphere (troposphere) %	in the human body %	Isotope mass number <i>A</i>	Relative abun- dance %	Atomic weight (physical scale)	Mode of decay ² Radi- ation	Energy in MeV	Half- life ³
90	Th	Thorium Thorium Thorium	232.05	4	1827	3530	solid 11.3	0.0025	—	—	227Th		RdAc	α γ	5.674...6.051 0.043...0.638	18.6 d
											228Th		RdTh	α γ	5.423/5.338 0.083/0.087	1.90 y
											230Th		Io	α γ	4.682/4.612 0.068/0.15 ...0.20	8 × 10 ⁴ y
											231Th		UY	β- γ	0.093/0.302/ 0.216 0.022/0.085/ 0.059	25.6 y
											232Th	100		α γ	3.98 0.055	1.39 × 10 ¹⁰ y
											234Th		UX _I	β- γ	0.192/0.104 0.090	24.10 d
91	Pa	Proto-actinium (Protactinium) Protactinium Protaktinium Protaktinium	231.0	—	—	—	—	6 × 10 ⁻¹²	—	—	231Pa	100		α γ	4.66/5.042 0.095/0.294/ 0.323	34,300 y
											234Pa		UX ₂	β- γ	2.32/0.8 1.5/0.782/ 0.822 0.394	1.14 m ↓ IT
													UZ	β- γ	0.45/1.2 0.782/0.822	6.7 h
92	U	Uranium Uranium Uran	238.07	3, 4, 6	1133	(3500?)	solid 18.68	6 × 10 ⁻⁴ 2 × 10 ⁻⁵	—	—	234U	0.0058		α γ	4.76 0.055	2.48 × 10 ⁵ y
											235U	0.71	AcU	α	4.40/4.58	7.1 × 10 ⁸ y
											238U	99.28	U _I	α	4.180	4.498 × 10 ⁹ y
														γ	0.045	

¹) From BRADFORD, J. R., in *Handbook of Chemistry and Physics*, Cleveland, 1954–55, pages 394–447.

²) α = alpha particle (helium nucleus = 2 protons + 2 neutrons), β⁻ = beta particle (negative electron), β⁺ = positron, γ = gamma ray, e⁻ = internal electron capture, K = orbital electron capture, IT = isomeric transition.

³) y = year, d = day, h = hour, m = minute, s = second.

⁴) Values in roman type apply to the earth's crust only; values in *italics* are total percentages in the lithosphere (outer 10 miles), hydrosphere and atmosphere (after REMY, H., *Lehrbuch der Anorganischen Chemie*, 7th edition, Leipzig, 1954).

Isotopes² (radiation/energy; half-life)

At. No.	Symbol	Element ¹	Atomic Weight	Valency	Isotopes ² (radiation/energy; half-life)
93	Np	Neptunium	(237)	3, 4, 5, 6	²³¹ Np ($\alpha/6.2$; K; 50 m), ²³² Np (γ , K; 13 m), ²³³ Np ($\alpha/5.53$; γ , K; 35 m), ²³⁴ Np ($\gamma/1.9$; K; 4.40 d), ²³⁵ Np ($\alpha/5.06$; K; 435 d), ²³⁶ Np ($\beta^-/0.51/0.36$; $\gamma/0.15$; K; 22 h), ²³⁷ Np ($\alpha/4.77$; $\gamma/0.065$; 2.2×10^6 y), ²³⁸ Np ($\beta^-/0.258/1.272$; $\gamma/0.983/0.047/1.030/0.043/0.103$; 2.10 d), ²³⁹ Np ($\beta^-/0.288/0.403/0.676$; $\gamma/0.0229$...0.277; 2.33 d), ²⁴⁰ Np ($\beta^-/ \sim 1.3$; 7.3 m), ²⁴¹ Np ($\beta^-/0.89$; γ ; 60 m)
94	Pu	Plutonium ³	(239)	3, 4, 5, 6	²³² Pu ($\alpha/6.6$; K; 36 m), ²³⁴ Pu ($\alpha/6.2$; K; 8.5 h), ²³⁵ Pu ($\alpha/5.85$; K; 26 m), ²³⁶ Pu ($\alpha/5.75$; $\gamma/0.045$; 2.7 y), ²³⁷ Pu (no γ ; K; 40 d), ²³⁸ Pu ($\alpha/5.49$; $\gamma/0.040$; 92 y), ²³⁹ Pu ($\alpha/5.147/5.1$; $\gamma/0.035/0.050$; 24,100 y), ²⁴⁰ Pu ($\alpha/5.16$; 6580 y), ²⁴¹ Pu ($\alpha/4.91$; $\beta^-/0.01$; 14 y), ²⁴² Pu ($\alpha/4.88$; 5×10^5 y), ²⁴³ Pu ($\beta^-/0.39$; $\gamma/0.095/0.12$; 5 h)
95	Am	Americium	(241)	2, 3, 4, 5	²³⁷ Am ($\alpha/6.01$; K; ~ 1.3 h), ²³⁸ Am (e^- ; K; 2.1 h), ²³⁹ Am ($\alpha/5.77$; $\gamma/0.285$; K; 12 h), ²⁴⁰ Am ($\alpha/1.3$; no γ ; K; 50 h), ²⁴¹ Am ($\alpha/5.476/5.433$; $\gamma/0.0597/0.100/0.041$; 475 y), ²⁴² Am ($\beta^-/0.628$; $\gamma/0.038/0.052$; $e^-/0.052$; K; 16 h IT $\rightarrow \alpha$; $\beta^-/0.58$; ~ 100 y), ²⁴³ Am ($\alpha/5.21$; $\sim 10^4$ y), ²⁴⁴ Am (β^- ; 25 m)
96	Cm	Curium	(242)	3	²³⁸ Cm ($\alpha/6.50$; 2.5 h), ²³⁹ Cm (K; ~ 3 h), ²⁴⁰ Cm ($\alpha/6.26$; K; 26.8 d), ²⁴¹ Cm ($\alpha/5.89$; K; 35.0 d), ²⁴² Cm ($\alpha/6.08$; $\gamma/0.045$; 162 d), ²⁴³ Cm ($\alpha/5.79/5.89$; 100 y), ²⁴⁴ Cm ($\alpha/5.78$; 19 y), ²⁴⁵ Cm (α ; > 500 y)
97	Bk	Berkelium	(243)	3, 4	²⁴³ Bk ($\alpha/6.72/6.55/6.20$; K; 4.6 h), ²⁴⁴ Bk (K; ~ 5 h), ²⁴⁵ Bk ($\alpha/6.15/5.90/6.33$; K; 4.95 d)
98	Cf	Californium	(244)	2	²⁴⁴ Cf ($\alpha/7.15$; K; 45 m), ²⁴⁶ Cf ($\alpha/6.75$; no K; 35.7 h)
99	E	Einsteinium	(?)		²⁵³ E ($\alpha/6.6$), ²⁵⁴ E
100	Fm	Fermium	(?)		²⁵⁴ Fm (α), ²⁵⁵ Fm ($\alpha/7.1$)
101	Mv	Mendelevium	(?)		

¹) The transuranic elements have become known as artificially-produced elements. However, since they have in the past occurred naturally (or are still, like Plutonium-239, identifiable in very small amounts in nature) they can be regarded also as naturally-occurring elements. In a sense they are elements which as a result of their short half-lives have become extinct.

²) From BRADFORD, J. R., in *Handbook of Chemistry and Physics*, Cleveland, 1954-55, pages 394-447, and other sources.

³) Total percentage natural abundance (see footnote⁴ opposite): 8×10^{-10} .

By HILDE LEVI, Ph. D.
Department of Biological Isotope Research, Zoophysiological Laboratory,
University of Copenhagen

Introduction

In recent years, artificial radio-isotopes have been produced in the United States, in Britain and although to a somewhat lesser extent on the continent of Europe in such quantities that their application in medicine and biology has made a multitude of new investigations possible.

Eight years after the release for research and therapy of radio-active material produced in the atomic piles, the tracer method developed by G. HEVESY has become an important tool, indispensable in any research laboratory or hospital. Innumerable designs of measuring equipment are commercially available, and these instruments have been built for a variety of special purposes. Just as is the case with any other method, it is a prerequisite for the successful application of radioactive tracers that we master the measuring technique and, moreover, are able properly to interpret the results of measurements. Investigations performed by means of isotopic tracers remain meaningless unless they are based on a thorough knowledge of the biological processes involved and of the basic principles of physics and chemistry.

Since users of these *Scientific Tables* will be familiar with medical and biological problems, the following tables give only a survey of the isotopes used in biological and medical research, together with

the nuclear data needed for the evaluation of the applicability and the radio-biological effect of these substances. In compiling the tables, a limited choice had to be made among the hundreds of artificial radio-isotopes now available. The tables contain only those isotopes which have been applied or are applicable to biological and medical research. This, in turn, depends on whether the element plays a part, if only a minor one, in the organism, and whether the physical properties of its radioactive isotope make its application feasible. Some radioactive isotopes which are interesting from a biological point of view decay so rapidly, i.e. in the course of seconds or minutes, that their short half-lives make them unsuited for biological experiments. Such isotopes have been omitted from the tables.

Furthermore, isotopes which have been used only as “trace elements” are not included. The possibility of detecting radio-isotopes in extremely low concentration, or high dilution, enables us to apply non-toxic quantities of these elements. In experiments on animals, numerous radio-isotopes of trace elements have been administered, their distribution in the organism and their excretion have been measured; however, no particularly striking conclusions have been drawn from these experiments.

Table 1
Nuclear data of the most important artificial radio-isotopes in medicine and biology²

Isotope	Half-life	Mode of decay	Maximum energy of β -radiation MeV	Mean energy of β -radiation MeV	Maximum range of β -radiation in H ₂ O mm	Energy of γ -radiation MeV	Fraction disintegrating per day
H- 3	12.4 y	β^-	0.018	0.006	0.003		2×10^{-4}
C- 11	20 m	β^+	0.98	0.38	4		1.0
C- 14	5570 y	β^-	0.155	0.05	0.3		4×10^{-7}
N- 13	10 m	β^+	1.25	0.48	5.6		1.0
F- 18	1.9 h	β^+	0.64	0.25	2.5		1.0
Na- 22	2.6 y	$\beta^+; \gamma$	0.57	0.2	2	1.3	7×10^{-4}
Na- 24	15.0 h	$\beta^-; \gamma$	1.4	0.54	6	1.38; 2.76	0.68
Si- 31	2.8 h	β^-	1.48	0.6	7		0.998
P- 32	14.3 d	β^-	1.7	0.68	8		0.05
S- 35	87 d	β^-	0.168	0.05	0.3		0.008
Cl- 36	4.5×10^5 y	β^-	0.7	0.24	2.5		5×10^{-9}
Cl- 38	37 m	$\beta^-; \gamma$	4.8; 2.8; 1.1	1.39	27	2.1; 1.6	1.0
K- 42	12.4 h	$\beta^-; \gamma$	3.6; 2.0	1.4	19	1.5	0.74
Ca- 45	152 d	β^-	0.26	0.09	0.6		0.004
Cr- 51	26.5 d	K				0.32	0.01
Mn- 52	6 d	$\beta^+; \gamma; K$	0.7	0.2	2.2	0.7; 0.9; 1.5	0.10
Mn- 54	310 d	K; γ				0.84	0.002
Fe- 55	2.9 y	K					6×10^{-4}
Fe- 59	46 d	$\beta^-; \gamma$	0.26; 0.46	0.12	1.6	1.1; 1.3	0.015
Co- 60	5.3 y	$\beta^-; \gamma$	0.32	0.1	0.8	1.16; 1.3	4×10^{-3}
Zn- 63	38 m	$\beta^+; \gamma; K$	2.36; 1.4	0.96	11	1.0; 1.9; 2.6	1.0
Zn- 65	250 d	$\beta^+; \gamma; K$	0.32	0.1	0.8	1.12	0.003
Br- 82	1.5 d	$\beta^-; \gamma$	0.46	0.15	1.4	0.55–2.0	0.4
Kr- 85	9.4 y	$\beta^-; \gamma$	0.7	0.2	2.5	0.54	2×10^{-4}
Sr- 89	54 d	β^-	1.48	0.55	7		0.013
I-131	8 d	$\beta^-; \gamma$	0.6	0.2	2	0.65; 0.8; 0.37	0.08
Au-198	2.7 d	$\beta^-; \gamma$	0.96; 0.29	0.34	3.8	0.41; 0.67	0.26

¹) Definitions of units: erg (erg) and mega-electron-volt (MeV), see page 61; millicurie (mc), microcurie (μ c) and röntgen (r), see page 70, röntgen-equivalent physical (rep), see page 71.

²) The data are from *Nuclear Data* (and Supplements 1950–51), National Bureau of Standards, and from *Table of Isotopes* by HOLLANDER, PERLMAN and SEABORG, *Rev. mod. Phys.*, **25**, 469, 1953.

Column six of Table 1 gives the maximum range of the β -component in water. This value is of interest when determining the amount of tissue irradiated after the radio-isotope is applied locally. The density of fresh tissue is simply set equal to that of water, i.e. equal to unity. If, for example, a given amount of phosphorus-32 is introduced as a point source into some soft tissue (in this connection, we have in mind an insoluble, non-metabolized compound), the surrounding tissue is irradiated to a distance of 8 mm from the point of application. Furthermore, the maximum range indicates the shielding required for complete absorption of the β -radiation. The last column lists the fraction of the

isotope which decays per day. This value enters the dosage calculation and is therefore repeated in Table 2.

It must be stressed here that half-lives and maximum energies of some isotopes are not yet finally determined. More exact and more recent measurements have yielded results which deviate from those obtained earlier. The values presented in the tables are taken from *Nuclear Data* (and Supplements), published by the National Bureau of Standards, Washington, 1949-51, and *Table of Isotopes* by J. M. HOLLANDER, I. PERLMAN and G. T. SEABORG, which give data as of December 1952.

Table 2
Dosimetry of some artificial radio-isotopes²

(1) Isotope	(2) Half-life T	(3) Fraction disintegrating per day f_d	(4) Mean energy of β -radiation \bar{E}_β (MeV)	(5) Dose factor K_β (rep)	(6) Tolerance concentration S_β ($\mu\text{c/kg}$)	(7) Critical organ	(8) Weight of critical organ (g)	(9) Max. permissible concentration in the total body (μc) ³
H- 3	12.4 y	2×10^{-4}	0.006	2400	140	total body	7×10^4	10^4
C- 11	20 m	1.0	0.38	0.47	106	—	—	—
C- 14	5570 y	4×10^{-7}	0.05	9×10^6	16	fat, bone	$10^4; 7 \times 10^3$	250; 1500
N- 13	10 m	1.0	0.48	0.3	167	—	—	—
F- 18	1.9 h	1.0	0.25	1.8	28	—	—	—
Na- 22	2.6 y	7×10^{-4}	0.22	18,000	4	—	—	—
Na- 24	15.0 h	0.68	0.54	29	2.5	total body	7×10^4	15
Si- 31	2.8 h	0.998	0.6	6	7.2	—	—	—
P- 32	14.3 d	0.05	0.68	860	1.16	bone	7×10^3	10
S- 35	87 d	0.008	0.05	380	15	skin	2×10^3	100
Cl- 36	4×10^5 y	5×10^{-9}	0.24	3×10^9	3	total body	7×10^4	200
Cl- 38	37 m	1.0	1.4	3.2	16	—	—	—
K- 42	12.4 h	0.74	1.4	70	1.0	muscle	3×10^4	20
Ca- 45	152 d	0.004	0.09	1200	10.5	bone	7×10^3	65
Cr- 51	26.5 d	0.025	0.01	20	100	kidney	300	390
Mn- 52	6 d	0.1	0.2	10	50	—	—	—
Mn- 54	310 d	0.002	0.005	135	185	—	—	—
Fe- 55	2.9 y	6×10^{-4}	0.006	570	140	blood	5×10^3	1000
Fe- 59	46 d	0.015	0.12	480	7	—	—	—
Co- 60	5.3 y	4×10^{-3}	0.1	17,000	7.4	liver	1.7×10^3	3
Zn- 63	38 m	1.0	0.96	2.3	22	—	—	—
Zn- 65	250 d	0.003	0.1	220	80	liver, bone	$1.7 \times 10^3; 7 \times 10^3$	430
Br- 82	1.5 d	0.46	0.15	20	6.4	—	—	—
Kr- 85	9.4 y	10^{-4}	0.2	60,000	8	—	—	—
Sr- 89	54 d	0.013	0.55	2600	1.5	bone	7×10^3	2
I-131	8 d	0.08	0.20	140	4.5	thyroid	20	0.3
Au-198	2.7 d	0.26	0.4	95	2.3	kidney	300	10

(3) Fraction of isotope disintegrating in 24 hours: $f_d = (1 - e^{-0.693/T})$, where T = half-life in days.
(4) For Cr-51, Mn-54 and Fe-55, the values \bar{E}_β include the total γ -radiation following decay by electron capture.
(5) $K_\beta = 88 \cdot \bar{E}_\beta \cdot T$ = dosage in rep for one microcurie completely disintegrated per gram of tissue.
(6) The tolerance concentration, in microcuries per kilogram of tissue, delivering the tolerance dose of 0.05 rep/day is $S_\beta = \frac{0.05 \times 1000}{K_\beta \times f_d}$
(7)-(9) From *Handbook 52* of the National Bureau of Standards, *Maximum Permissible Amounts of Radioisotopes in the Human Body and Maximum Permissible Concentrations in Air and Water*, U.S. Department of Commerce, National Bureau of Standards, issued March 20th, 1953.

Table 2 gives the data necessary for dosage calculations, the tolerance concentration in microcuries per kilogram of tissue, and the maximum permissible concentrations of some radio-isotopes in the human body for continuous radiation. The values in columns 7, 8 and 9 are taken directly from *Handbook 52* of the National Bureau of Standards (see above). A more detailed discussion of the tolerance problem would fall beyond the scope of the present survey, but it may be mentioned briefly that the toler-

¹) Definitions of units: erg (erg) and mega-electron-volt (MeV), see page 61; millicurie (mc), microcurie (μc) and röntgen (r), see page 70, röntgen-equivalent physical (rep), see page 71.
²) In the calculation of the tolerance concentration S_β , the β -component only is taken into account. The values of K_β and S_β have been recalculated on the basis of the data listed in Table 1. The dose factors of a number of γ -emitting isotopes are given in Table 3.

ance dose 0.3 r (or 0.3 rep) per working week (generally 40 hours) forms the basis for the calculations. This value for the tolerance dose is at present recognized in most countries. It is, however, not final. At the Seventh International Congress of Radiology in Copenhagen, 1953, the value of 0.3 rep per working week was accepted; suggestions to change this value tend towards a lower value for the tolerance dose. (For definition of this and similar units, see page 71.)

Columns two, three and four of Table 2 give the half-lives, the fractions decaying per day, and the mean energies of the β -radiation. The dosage factor K_β is calculated according to the equation $K_\beta = 88 \cdot \bar{E}_\beta \cdot T$, where \bar{E}_β is the mean energy of the β -radiation, T the half-life in days; the factor 88 accounts, *inter alia*, for the conversion of MeV into the energy unit erg. Thus, the dose factor gives the dosage (in rep) for one microcurie completely disintegrated per gram of tissue (column five). The tolerance concentration is listed in column six. It is assumed that the isotopes listed in column one are distributed uniformly in a kilogram of tissue. On this assumption, it has been calculated which concentration of the respective isotopes will deliver to this tissue mass the tolerance dose of 0.05 rep per day. (The value of 0.05 rep = $\frac{1}{6}$ of the weekly dose, is likewise a rough approximation.) It is obvious that the values for S_β can only serve for orientation, particularly as very few substances are distributed uniformly in the tissue. For some elements, for example iodine and calcium, the tissue mass in which the isotope is preferentially accumulated is known; it therefore becomes possible to estimate how many microcuries

can be introduced into the body without exceeding the tolerance level in the respective tissue. On the basis of similar considerations tables have been presented in the literature which contain values for the permissible tracer level. This term refers to the quantity of a given isotope in microcuries which can be introduced into the human organism without at any time and in any tissue exceeding the tolerance concentration. A reliable calculation of such "permissible" tracer concentrations requires, however, that numerous biological and physico-chemical factors are taken into account (resorption and retention, rate of excretion, density of the tissue, distribution, etc.). In the author's view, a publication of this kind from a really competent team of scientists is not yet available. The International Radiological Commissions have, however, published "recommendations" (*Recommendations of the International Commission on Radiological Protection and of the International Commission on Radiological Units*²). A subcommittee of these commissions has collected and published the most reliable data in this field in *Handbook 52 of the National Bureau of Standards* under the title *Maximum Permissible Amounts of Radioisotopes in the Human Body and Maximum Permissible Concentrations in Air and Water*. Columns 7, 8 and 9 of Table 2 are taken directly from this handbook. (N.B. These values hold for continuous irradiation.)

In order to facilitate the estimation of tolerance concentrations, Tables 4 and 5 give some data for the "standard man" on which the calculations of the International Radiological Commissions are based. These tables have been taken directly from *NBS Handbook 47* and from a more recent publication by the Commissions in Supplement 6 to the *British Journal of Radiology*, 1955.

Table 3
Dose rates from a 1 mc point source of some γ -emitting isotopes³

Isotope	Half-life	γ -Energy in MeV	Dose rate in mr/h from 1 mc at 1 m	Dose rate in r/h from 1 mc at 1 cm
Na-22	2.6 y	1.3	1.3	13.2
Na-24	15 h	1.38; 2.7	1.9	19.1
Cl-38	37 m	1.6; 2.1	0.76	7.6
K-42	12.4 h	1.5	0.19	1.9
Mn-52	6 d	0.7; 0.9; 1.5	1.9	19.5
Mn-56	2.6 h	1.7; 2.06	0.94	9.4
Fe-59	46 d	1.1; 1.3	0.65	6.55
Co-60	5.3 y	1.17; 1.3	1.35	13.5
Zn-63	38 m	1.0; 1.9; 2.6	0.69	6.9
Br-82	1.5 d	0.5 to 2.0	1.5	15.1
I-131	8 d	0.37; 0.65; 0.8	0.26	2.65
Au-198	2.7 d	0.41; 0.67	0.24	2.4

Since the most recent values for the γ -energies differ only slightly from the values used by QUIMBY, the dose rates have been reproduced unchanged.

¹) Definitions of units: erg (erg) and mega-electron-volt (MeV), see page 61; millicurie (mc), microcurie (μ c) and röntgen (r), see page 70, röntgen-equivalent physical (rep), see page 71.
²) Published by the U.S. Department of Commerce, as Handbook 47 of the National Bureau of Standards, and obtainable from the Superintendent of Documents, Government Printing Office, Washington 25, D.C.
³) QUIMBY, E. H., *Dosimetry of Internally Administered Radioactive Isotopes*, in *Manual of Artificial Radioisotope Therapy*, edited by P. HAHN, New York, 1951.

Table 4
Weight distribution in the standard man¹
(total body weight 70 kg)

Organ	Weight in grams	Organ	Weight in grams
Muscles	30,000	Heart	300
Skeleton:		Lymphoid tissue	700
Bones	7000	Brain	1500
Red marrow	1500	Spinal cord	30
Yellow marrow	1500	Bladder	150
Blood	5000	Salivary glands	50
Gastrointestinal tract	2000	Eyes	30
Lungs	1000	Teeth	20
Liver	1700	Prostate	20
Kidney	300	Adrenals	20
Spleen	150	Thymus	10
Pancreas	70	Skin and subcutaneous tissues	8500
Thyroid	20	Other tissues and organs not separately defined	8390
Testes	40		

Table 5
Other data pertaining to the standard man (total body weight 70 kg)

Chemical composition of the body^a

Element	Percentage of total body weight	Total weight g
Oxygen	65.0	45,500
Carbon	18.0	12,600
Hydrogen	10.0	7000
Nitrogen	3.0	2100
Calcium	1.5	1050
Phosphorus	1.0	700
Sulphur	0.25	175
Potassium	0.2	140
Sodium	0.15	105
Chlorine	0.15	105
Magnesium	0.05	35
Iron	0.006	4
Copper	0.0002	0.1
Manganese	0.00003	0.02
Iodine	0.00004	0.03

Water balance¹

	Millilitres per day
Daily water intake:	
In food (including 300 ml water of oxidation) .	1000
As fluids	1500
Total water	2500
Total water intake	2200
Daily water output:	
Sweat	500
From lungs	400
In faeces	100
Urine	1500
Total	2500
Respiration:	
8 hours at work	10 × 10 ⁶
16 hours not at work	10 × 10 ⁶
24 hours	20 × 10 ⁶

¹) From Handbook 47, *Recommendations of the International Commission on Radiological Protection and of the International Commission on Radiological Units*, U.S. Department of Commerce, National Bureau of Standards, 1950. These data have been used in the calculation of the maximum permissible concentration of radio-isotopes in the body.
²) From *Brit. J. Radiol.*, Supplement 6, 1955.

Table 6
Applications of radio-isotopes

Application, or suggested application, in medicine	Isotope	Application in biological and physiological research
	Hydrogen H-3	Body water content.
	Carbon C-11 C-14	CO ₂ metabolism. Application of C-14 labelled compounds to metabolic studies (localization, reaction mechanism, retention or lifetime, metabolic pool of a substance by means of the isotope dilution method). Carbohydrate, fat, albumin, amino-acid metabolism.
	Nitrogen N-13	Respiratory gas exchange.

Table 6 (continued)

Application, or suggested application, in medicine	Isotope	Application in biological and physiological research
Therapy: whole body irradiation, erythropoiesis, polyglobuly.	Fluorine F-18	Physiology and chemistry of bones and teeth.
Diagnosis: circulation measurements with Na-24 labelled plasma. Determination of the extravascular space according to the dilution method. Blood circulation in extremities and organs. Cardiac insufficiency.	Sodium Na-24	(Also Na-22) Excretion, resorption; permeability of capillaries, gastric mucosa, intestinal walls, placenta, organic cell walls. Distribution between plasma and tissue. Ion transport.
Therapy: surface therapy of deformities and malformations, skin lesions, eczema. Chronic leukaemia and polycythaemia. Selective irradiation with colloids containing P-32.	Phosphorus P-32	Mineral metabolism, intermediary metabolism.
Diagnosis: blood volume determinations and circulation diagnosis with P-32 labelled erythrocytes.		
Therapy: experiments with selective irradiation of the joints.	Sulphur S-35	Permeability studies. Intermediary metabolism. Metabolism of sulphur-containing amino-acids and peptides, S-35 labelled pharmaceuticals. Mineral metabolism.
Diagnosis: recent investigations regarding sulphur accumulation in tumours.		
	Chlorine Cl-36 Cl-38	Mineral metabolism, permeability, ion transport through membranes.
	Potassium K-42	Mineral metabolism, adrenal physiology.
	Calcium Ca-45	Mineral metabolism, incorporation of Ca in the bones of rachitic and vitamin-D treated animals. Bone healing.
Diagnosis: blood volume and circulation studies with Cr-51 labelled erythrocytes.	Chromium Cr-51	Plasma-albumin investigations with ⁵¹ CrCl ₃ .
Therapy: local irradiation of lymph nodes. Distribution of colloidal MnO ₂ in the reticuloendothelial system.	Manganese Mn-52 Mn-54	Mineral metabolism.
Diagnosis: blood volume; lifetime of erythrocytes.	Iron Fe-55 Fe-59	Mineral metabolism, blood physiology, resorption by gastric and intestinal mucosa. Distribution of Fe in the organism. Blood preservation.
Therapy: telecurie therapy, external (high depth doses). Co-wire for local application. Intracavitary cobalt chloride solution in rubber bags as cavity applicator (bladder).	Cobalt Co-60	Mineral metabolism.
Therapy: intratumoral therapy. Zn-63 as insoluble sulphide and as sol; intraperitoneal and intrapleural application. Zn-63 in coarse-disperse sulphide form results in selective fixation in the lungs.	Zinc Zn-63 Zn-65	Mineral metabolism. Lifetime of leucocytes.
	Bromine Br-82	Electrolyte exchange. Thyroid physiology, distribution of brominated dyes.
Diagnosis: minute-volume determination.	Krypton Kr-85	Respiratory gas exchange.
Therapy: therapy of bone sarcoma.	Strontium Sr-89	Absorption-distribution-excretion. Bone physiology.
Therapy: selective irradiation of the thyroid. Treatment of hyperthyroidism, thyroid carcinoma, diffuse and nodular struma.	Iodine I-131	Iodine metabolism. Thyroid physiology.
Diagnosis: thyroidal dysfunction. Localization of tumours by means of I-131-diiodofluorescin.		
Therapy: in insoluble form (pectin sol) for intracavitary treatment. Peritoneal and pleuro-carcinosis. Intratumoral therapy.	Gold Au-198	Absorption-distribution-excretion; distribution in arthritis.

Table 6 presents a survey of the radio-isotopes used in medicine and biology. Under medical application, therapy and diagnosis are listed separately, while medico-physiological tracer investigations are given under biology. The literature available in this field is so extensive that any attempt at referring to the original papers would necessarily lead to an incomplete and thus unfair review of the investigations which have been performed.

Acetanilide	$C_6H_5NHCOCH_3$	135.16	Ethyl alcohol	C_2H_5OH	46.07
Acetophenetidin. See Phenacetin			Ethylmorphine hydrochloride	$[C_{18}H_{23}O_3N]HCl + 2H_2O$	385.88
Acetylcholine chloride	$[CH_3COOCH_2CH_2N(CH_3)_3]Cl$	181.66	<i>N</i> -Ethylpiperidine	$CH_3CH_2CH_2CH_2CH_2NC_2H_5$	113.20
Acetylsalicylic acid	$C_9H_8(OOH)(OCOCH_3)-1,2$	180.15			
Aconitine	$C_{34}H_{48}O_{11}N$	647.74	Eucalyptol	$(CH_3)_2CCHCH_2CH_2C(O)(CH_3) \cdot CH_2CH_3$	154.24
Adrenaline, epinephrine (hydrochloride)	$C_9H_9[CH(OH)CH_2NHCH_3][OH]_2 \cdot HCl-1,3,4$	219.67			
Allyl isothiocyanate	$CH_3 \cdot CHCH_2NCS$	99.15	Eucatropine	$C_6H_5CH(OH)COOCHCH_2C(CH_3)_2N(CH_3)CH(CH_3)CH_2$	291.38
Amidopyrine. See Aminopyrine			Formaldehyde	$HCHO$	30.03
Aminophylline			Girard's reagent	$[(CH_3)_3NCH_2CONHNH_2]Cl$	167.64
	$[N(CH_3)CON(CH_3)C : CCON : CHNH]_2 \cdot NH_2CH_2CH_2NH_2 + 2H_2O$	456.46	Glycerol	$HOCH_2CH(OH)CH_2OH$	92.09
Aminopyrine, dimethyl-aminoantipyrine, aminophenazone	$N(C_6H_5)N(CH_3)C(CH_3) : C[N(CH_3)_2]CO$	231.29	Histamine	$N : CHNHCH : CCH_2CH_2NH_2$	111.15
Amphetamine	$C_6H_5CH_2CH(NH_2)CH_3$	135.20	Homatropine	$C_{16}H_{21}O_3N$	275.34
Amyl nitrite	$(CH_3)_2CHCH_2CH_2ONO$	117.15	Hyoscyamine	$C_{17}H_{23}O_3N$	289.36
Antimony			Iodoform	CHI_3	393.78
potassium tartrate (tartar emetic)	$[KOOC(CHOH)_2COOSbO] + \frac{1}{2}H_2O$	333.94	Lactic acid	$CH_3CH(OH)COOH$	90.08
Antipyrin	$N(C_6H_5)N(CH_3)C(CH_3) : CHCO$	188.22	Lanatoside C	$C_{49}H_{76}O_{20}$	985.10
Apomorphine hydrochloride	$[C_{17}H_{17}O_2N \cdot HCl] + \frac{1}{2}H_2O$	312.79	Mandelic acid	$C_6H_5CH(OH)COOH$	152.14
Atropine	$C_{17}H_{23}O_3N$	289.36			
Barbitone, diethylbarbituric acid	$NHCONHCOC(C_2H_5)_2CO$	184.19	Menthol	$(CH_3)_2CHCHCH(OH)CH_2CH(CH_3)CH_2CH_3$	156.26
Barbitone sodium	$NHC(ONa) : NCOC(C_2H_5)_2CO$	206.18	Mepacrine (quinacrine)	$C_{28}H_{30}ClON_8$	399.95
Bromoform	$CHBr_3$	252.77	Meperidine	$C_6H_5 \cdot C(COOC_2H_5) \cdot CH_2CH_2N(CH_3)CH_2CH_3$	247.33
Butacaine sulphate	$[H_2NC_6H_4COO(CH_2)_3N(C_4H_9)_2-1,4]_2 \cdot H_2SO_4$	710.95	Methyl alcohol	CH_3OH	32.04
			Methylene blue	$[C_{16}H_{18}ClN_3S] + 3H_2O$	373.90
Caffeine	$[N(CH_3)CON(CH_3)C : CCO : N : CHN(CH_3)] + H_2O$	212.21	Morphine	$[C_{17}H_{19}O_3N] + H_2O$	303.35
Calcium gluconate	$[[CH_2OH(CHOH)_4COO]_2Ca] + H_2O$	448.39	Neostigmine bromide	$C_6H_4[N(CH_3)_3Br][OCON(CH_3)_2]-1,3$	303.20
- glycerophosphate	$[C_3H_5(OH)_2OPO_3Ca] + H_2O$	228.16	Nikethamide (coramine)	$CH : CHCH : NCH : CCON(C_2H_5)_2$	178.23
- lactate	$[[CH_3CH(OH)COO]_2Ca] + 5H_2O$	308.30	Nitrogen mustard. See Allyl isothiocyanate		
- mandelate	$[C_6H_5CH(OH)COO]_2Ca$	342.35	Ouabain, strophanthin-G	$[C_{20}H_{44}O_{12}] + 8H_2O$	728.77
Camphor	$C(CH_3)CH_2CH_2CHC(CH_3)_2CH_2CO$	152.23	Papaverine	$C_{20}H_{21}O_4N$	339.38
Carbarsone	$C_6H_4[AsO(OH)_2][NHCONH_2]-1,4$	260.07	Penicillin-G sodium	$C_{16}H_{17}N_2NaO_4S$	356.38
Carbromal	$(C_2H_5)_2CBrCONHCONH_2$	237.11	Pentobarbitone	$NHCONHCOC[CH(CH_3)_2C_6H_7][C_2H_5]CO$	226.27
Chloral hydrate	$CCl_3CH(OH)_2$	165.42	Phenacetin, acetophenetidin	$C_6H_4(NHCOCH_3)(OC_2H_5)-1,4$	179.21
Chloramphenicol	$CH(OH)(C_6H_4-p-NO_2) \cdot CH(NHCOCHCl_2) \cdot CH_2OH$	323.14	Phenazone. See Antipyrin		
Chloroform	$CHCl_3$	119.39	Phenobarbitone	$NHCONHCOC(C_6H_5)(C_2H_5)CO$	232.23
Chloromycetin. See Chloramphenicol			- sodium	$NHC(ONa) : NCOC(C_6H_5)(C_2H_5)CO$	254.22
Chloroquine	$C_9H_5N[Cl][NHCH(CH_3) \cdot (CH_2)_3 \cdot N(C_2H_5)_2]-7,4$	319.87	Physostigmine	$C_{16}H_{21}O_2N_3$	275.34
Cholesterol	$C_{27}H_{48}OH$	386.64	Picrotoxin	$C_{30}H_{44}O_{13}$	602.57
Cinchophen	$CH : CH \cdot CH : CH \cdot C : C \cdot C(COOH) : CH \cdot C(C_6H_5) : N$	249.26	Pilocarpine	$C_{11}H_{16}O_2N_2$	208.26
Cocaine	$C_{17}H_{21}O_4N$	303.35	Piperocaine	$C_6H_5COO(CH_2)_3N \cdot (CH_2)_4 \cdot CH(CH_3)$	261.36
Codeine	$[C_{18}H_{21}O_3N] + H_2O$	317.37	Procaine hydrochloride	$C_6H_4[COOCH_2CH_2N(C_2H_5)_2][NH_2] \cdot HCl-1,4$	272.77
Colchicine	$C_{22}H_{25}O_6N$	399.43	Quinacrine. See Mepacrine		
Coumarin	$CH : CHCH : CHC : C \cdot O \cdot CO \cdot CH : CH$	146.14	Quinidine	$C_{20}H_{24}O_2N_2$	324.41
			Quinine	$[C_{20}H_{24}O_2N_2] + 3H_2O$	378.46
Creatinine	$CH_3NC : (NH)NHCOCH_2$	113.12	Resorcinol	$C_6H_4(OH)_2-1,3$	110.11
Cresol	$CH_3C_6H_4OH$	108.13	Rochelle salt (potassium sodium tartrate)	$[CH(OH)(COOK) \cdot CH(OH)(COONa)] + 4H_2O$	282.23
Cyclopropane	$CH_2CH_2CH_2$	42.08	Rutin	$[C_{27}H_{30}O_{16}] + 3H_2O$	664.56
Dextrose (D-glucose)	$[CH_2(OH) \cdot CH(OH) \cdot CH(OH) \cdot (HO)CH \cdot CH(OH) \cdot CHO] + H_2O$	198.17	Salicylic acid	$C_6H_4(COOH)(OH)-1,2$	138.12
Diethylbarbituric acid. See Barbitone			Santonin	$CH : CH \cdot CO \cdot C(CH_3) : C \cdot C(CH_3) \cdot CH_2 \cdot CH_2 \cdot CH \cdot CH \cdot O \cdot CO \cdot CH \cdot CH_3$	246.30
Diethylstilboestrol. See Stilboestrol			Scopolamine	$C_{17}H_{21}O_4N$	303.35
Digitonin	$C_{55}H_{90}O_{20}$	1215.27	Sodium lactate	$CH_3CH(OH)COONa$	112.07
Digitoxin	$C_{41}H_{64}O_{13}$	764.92	Stilboestrol	$p-HOC_6H_4(C_2H_5)C : C(C_2H_5)C_6H_4OH-p'$	268.34
Dihydromorphinone	$C_{17}H_{19}O_3N$	285.33	Streptomycin hydrochloride	$C_{21}H_{39}O_{12}N_7 \cdot 3HCl$	690.98
Dihydrostreptomycin	$C_{21}H_{41}O_{12}N_7$	583.59	- sulphate	$(C_{21}H_{39}O_{12}N_7)_2 \cdot 3H_2SO_4$	1457.40
- hydrochloride	$C_{21}H_{41}O_{12}N_7 \cdot 3HCl$	692.99	Strophanthin-G. See Ouabain		
- sulphate	$(C_{21}H_{41}O_{12}N_7)_2 \cdot 3H_2SO_4$	1461.43	Strychnine	$C_{21}H_{22}O_8N_2$	334.40
Diiodohydroxyquinoline	$CJ : CHCJ : C(OH)C : CCH : CHCH : N$	396.98	Sulphadiazine	$p-NH_2 \cdot C_6H_4 \cdot SO_2NHC : N \cdot CH : CH \cdot CH : N$	250.28
Dimercaprol	$CH_2(SH)CH(SH)CH_2OH$	124.23	Sulphamerazine	$p-NH_2 \cdot C_6H_4 \cdot SO_2NHC : N \cdot CH : CH \cdot C(CH_3) : N$	264.30
<i>m</i> -Dinitrobenzene	$C_6H_4(NO_2)_2-1,3$	168.11	Sulphanilamide	$p-NH_2 \cdot C_6H_4 \cdot SO_2NH_2$	172.21
Dioxan	$OCH_2CH_2OCH_2CH_2$	88.10	Sulphapyridine	$p-NH_2 \cdot C_6H_4 \cdot SO_2NHC : N \cdot CH : CH \cdot CH : CH$	249.29
Diphenylhydantoin	$(C_6H_5)_2CNHCONHCO$	252.26	Sulphathiazole	$p-NH_2 \cdot C_6H_4 \cdot SO_2NHC : N \cdot CH : CH \cdot S$	255.32
Emetine hydrochloride	$C_{29}H_{40}O_4N_2 \cdot 2HCl$	553.56	Theobromine	$NH \cdot CO \cdot N(CH_3) \cdot C : C : CO \cdot N : CH \cdot NCH_3$	180.17
Ephedrine hydrochloride	$C_6H_5CH(OH)CH(NHCH_3)CH_2 \cdot HCl$	201.69	Theophylline	$N(CH_3) \cdot CO \cdot N(CH_3) \cdot C : C : CO \cdot N : CH \cdot NH \cdot H_2O$	198.18
Ergonovine	$C_{19}H_{23}O_2N_3$	325.40	Tryparsamide	$[p-NH_2COCH_2NH \cdot C_6H_4AsO(OH)ONa] + \frac{1}{2}H_2O$	305.09
Ergotamine	$C_{33}H_{35}N_5O_6$	581.65	Tubocurarine hydrochloride	$[C_{38}H_{44}Cl_2O_6N_2] + 5H_2O$	785.74
- tartrate	$(C_{33}H_{35}N_5O_6)_2 \cdot H_2C_4H_4O_6$	1313.39	Undecylenic acid	$CH_2 : CH \cdot (CH_2)_8 \cdot COOH$	184.27
Ergotoxine	$C_{35}H_{41}O_6N_5$	627.72	Urea (carbamide)	$CO(NH_2)_2$	60.06
Ether	$(C_2H_5)_2O$	74.12	Urethane	$H_2NCOOC_2H_5$	89.09
			Uric acid	$NH \cdot CO \cdot NH \cdot C : C \cdot CO \cdot NH \cdot CO \cdot NH$	168.11

Substance	Molecular weight	Hydrogen equivalent	1 ml of 0.1-N solution contains (gram)	Mantissa of log ₁₀ * of equivalent weight
Acetic acid	60.03	CH ₃ COOH	0.006003	7784
Ammonia	17.03	NH ₃	0.001703	2311
Ammonium chloride	53.50	NH ₄ Cl	0.005350	7284
Ammonium hydroxide	35.05	NH ₄ OH	0.003505	5447
Ammonium nitrate	80.05	NH ₄ NO ₃	0.008005	9034
Ammonium sulphate	132.14	½(NH ₄) ₂ SO ₄	0.006607	8200
Ammonium thiocyanate	76.12	NH ₄ CNS	0.007612	8815
Barium carbonate	197.36	½BaCO ₃	0.009868	9943
Barium chloride	244.31	½[BaCl ₂ +2H ₂ O]	0.012216	0869
Barium hydroxide	315.51	½[Ba(OH) ₂ +8H ₂ O]	0.015775	1979
Barium oxide	153.36	½BaO	0.007668	8847
Boric acid	61.84	⅓H ₃ BO ₃	0.002061	3141
Bromine	159.84	½Br ₂	0.007992	9026
Calcium carbonate	100.08	½CaCO ₃	0.005004	6993
Calcium chloride	110.99	½CaCl ₂	0.005550	7442
Calcium chloride hexahydrate	219.09	½[CaCl ₂ +6H ₂ O]	0.010955	0396
Calcium hydroxide	74.10	½Ca(OH) ₂	0.003705	5688
Calcium oxide	56.08	½CaO	0.002804	4478
Carbon dioxide	44.01	½CO ₂	0.002201	3424
Chlorine	70.91	½Cl ₂	0.003546	5496
Citric acid	210.08	⅓[C ₆ H ₈ O ₇ +H ₂ O]	0.007003	8452
Copper oxide	79.57	½CuO	0.003979	5997
Copper sulphate	249.71	½[CuSO ₄ +5H ₂ O]	0.012485	0964
Hydriodic acid	127.93	HI	0.012793	1069
Hydrobromic acid	80.92	HBr	0.008092	9080
Hydrochloric acid	36.47	HCl	0.003647	5619
Hydrocyanic acid	27.02	HCN	0.002702	4317
Iodine	253.84	½I ₂	0.012692	1035
Lactic acid	90.05	CH ₃ ·CHOH·COOH	0.009005	9544
Lead carbonate	267.22	½PbCO ₃	0.013361	1258
Lead oxide	223.21	½PbO	0.011161	0477
Magnesium carbonate	84.32	½MgCO ₃	0.004216	6249
Magnesium chloride	95.23	½MgCl ₂	0.004762	6777
Magnesium chloride hexahydrate	203.33	½[MgCl ₂ +6H ₂ O]	0.010167	0071 ₉₂₈
Magnesium oxide	40.32	½MgO	0.002016	3045
Malic acid	134.09	½C ₄ H ₆ O ₅	0.006704	8264
Manganese sulphate	150.99	½MnSO ₄	0.007550	8779
Mercuric chloride (Sublimate)	271.52	½HgCl ₂	0.013576	1327
Nitric acid	63.02	HNO ₃	0.006302	7994
Nitrous acid	47.02	HNO ₂	0.004702	6723
Oxalic acid	90.02	½HOOC·COOH	0.004501	6533
Oxalic acid dihydrate	126.05	½[HOOC·COOH+2H ₂ O]	0.006303	7995
Phosphoric acid	98.04	⅓H ₃ PO ₄	0.003268	5143
Potassium bicarbonate	100.11	KHCO ₃	0.010011	0004 ₇₂₁
Potassium bitartrate	188.18	C ₄ H ₅ O ₆ K	0.018818	2745
Potassium carbonate	138.20	½K ₂ CO ₃	0.006910	8395
Potassium chloride	74.55	KCl	0.007455	8725
Potassium cyanide	65.11	KCN	0.006511	8137
Potassium dichromate	294.21	⅓K ₂ Cr ₂ O ₇	0.004904	6905
Potassium hydroxide	56.11	KOH	0.005611	7491
Potassium oxide	94.20	½K ₂ O	0.004710	6730
Potassium permanganate for CO determination	158.03	⅓KMnO ₄	0.003161	4998
Potassium permanganate for Mn determination	158.03	⅓KMnO ₄	0.005268	7216
Potassium tartrate	226.23	½C ₄ H ₄ O ₆ K ₂	0.011312	0536
Potassium tetroxalate	254.19	⅓[KH ₃ (C ₂ O ₄) ₂ +2H ₂ O] ₂	0.008473	9281
Silver nitrate	169.89	AgNO ₃	0.016989	2302
Sodium bicarbonate	84.00	NaHCO ₃	0.008400	9243
Sodium carbonate	105.99	½Na ₂ CO ₃	0.005300	7243
Sodium chloride	58.45	NaCl	0.005845	7668
Sodium hydroxide	40.00	NaOH	0.004000	6021
Sodium oxide	61.99	½Na ₂ O	0.003100	4913
Sodium phosphate (Disodium phosphate)	178.05	½[Na ₂ HPO ₄ +2H ₂ O]	0.008902	9495
Sodium phosphate (Trisodium phosphate)	380.21	⅓[Na ₃ PO ₄ +12H ₂ O]	0.012674	1029
Sodium sulphide	78.05	½Na ₂ S	0.003903	5914
Sodium tetraborate	201.27	½Na ₂ B ₄ O ₇	0.010064	0027 ₇₇₈
Sodium tetraborate (Borax)	381.44	½[Na ₂ B ₄ O ₇ +10H ₂ O]	0.019072	2804
Succinic acid	118.05	½C ₄ H ₆ O ₄	0.005902	7711
Sulphuric acid	98.08	½H ₂ SO ₄	0.004904	6906
Sulphur trioxide	80.06	½SO ₃	0.004003	6024
Tartaric acid	150.05	½C ₄ H ₆ O ₆	0.007502	8752
Zinc sulphate	287.55	½[ZnSO ₄ +7H ₂ O]	0.014378	1577

* Logarithms, see pages 8–11.

The solutions must be prepared with distilled water free from carbon dioxide and with pure reagents.

Buffer		pH Range	Stock solution A	Stock solution B	Composition of the mixture
1	KOLTHOFF's borax-succinic acid	3.0 ... 5.8	0.05 molar borax (19.1 g/l)	0.05 molar succinic acid (5.9 g/l)	A + B = 100 ml
2	CLARK and LUBS' boric acid	7.8 ...10.0	0.1 molar boric acid (6.18 g/l)	0.1 molar NaOH (4 g/l)	100 ml A + ∞ ml B
3	KOLTHOFF's borax-monopotassium phosphate	5.8 ... 9.2	0.05 molar borax (19.1 g/l)	0.1 molar KH ₂ PO ₄ (13.62 g/l)	A + B = 100 ml
4a	SÖRENSEN's sodium citrate	2.2 ... 4.2	21.008 g citric acid (C ₆ H ₈ O ₇ ·H ₂ O) and 200 ml 1-N NaOH, diluted to 1 liter	a) 0.1-N HCl	A + B = 100 ml
4b		5.0 ... 6.4		b) 0.1-N NaOH (4.0 g/l)	A + B = 100 ml
5	McILVAINE's citric acid-phosphate	2.2 ... 8	0.2 molar Na ₂ HPO ₄ (35.6 g Na ₂ HPO ₄ ·2H ₂ O per liter)	0.1 molar citric acid (21.01 g C ₆ H ₈ O ₇ ·H ₂ O/liter)	A + B = 100 ml
6a	SÖRENSEN's glycine	1.08... 3.4	7.505 g glycine + 5.85 g NaCl diluted to 1 liter (0.1 molar glycine + 0.1 molar NaCl)	a) 0.1-N HCl	A + B = 100 ml
6b		9.0 ...13		b) 0.1-N NaOH	A + B = 100 ml
7a	CLARK and LUBS' potassium acid phthalate	2.2 ... 3.8	0.1-N potassium acid phthalate (20.418 g/l)	a) 0.1-N HCl	100 ml A + ∞ ml B in 200 ml
7b		4.0 ... 6.2		b) 0.1-N NaOH	
8	CLARK and LUBS' potassium chloride-hydrochloric acid	1.2 ... 2.2	0.2-N KCl (14.92 g/l)	0.2-N HCl	100 ml A + ∞ ml B in 400 ml
9	SÖRENSEN's phosphate	5.4 ... 8.0	¹ / ₁₅ molar KH ₂ PO ₄ (9.078 g/l)	¹ / ₁₅ molar Na ₂ HPO ₄ ·2H ₂ O (11.876 g/l)	A + B = 100 ml
10	MICHAELIS's barbital	6.8 ... 9.6	0.1 molar barbital sodium (20.62 g/l)	0.1-N HCl	A + B = 100 ml
11	THEORELL and STENHAGEN's	2.0 ...12.0	To citric acid and phosphoric acid solutions (about 100 ml) each corresponding to 100 ml 1-N NaOH, are added 3.54 g cryst. boric acid and 343 ml 1-N NaOH, and the mixture diluted to 1 liter	0.1-N HCl	100 ml A + ∞ ml B in 500 ml

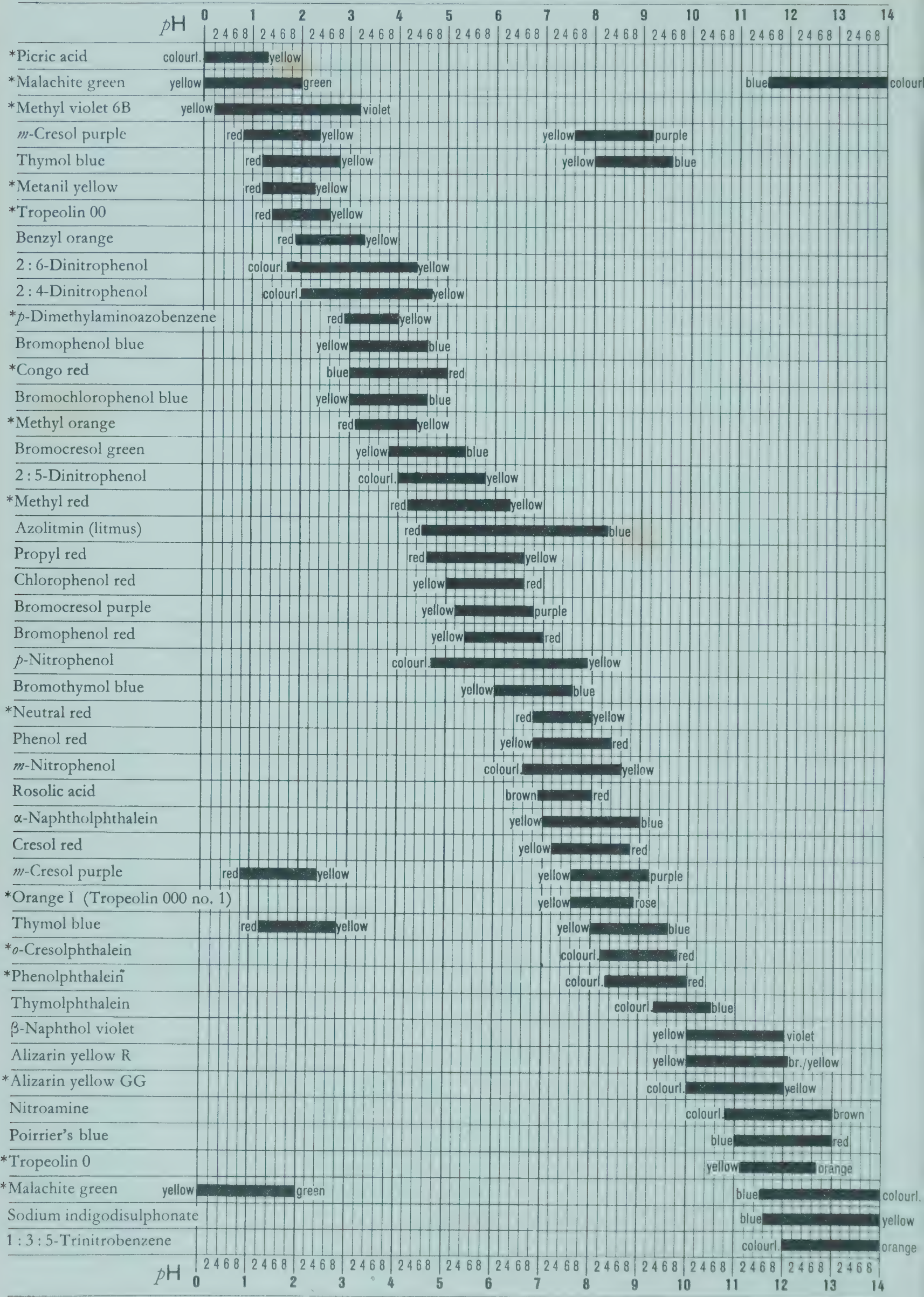
pH Values of buffer solutions at 18° C

The table gives the required volumes (in milliliters) of solution B in the above mixtures. An asterisk indicates that A + B is not equal to 100.

pH	1	2	3	4a	4b	5	6a	7a	7b	8	11
1.08	—	—	—	—	—	—	100	—	—	—	—
1.2	—	—	—	—	—	—	85	—	—	129*	—
4	—	—	—	—	—	—	71	—	—	83*	—
6	—	—	—	—	—	—	62	—	—	52.6*	—
8	—	—	—	—	—	—	54	—	—	33.2*	—
2.0	—	—	—	—	—	—	48	—	—	21.2*	366.5*
2	—	—	—	67.2	—	98.0	42	93.4*	—	13.4*	339.3*
4	—	—	—	65.2	—	93.8	36	79.2*	—	—	319.3*
6	—	—	—	63.5	—	89.1	30	65.9*	—	—	304.0*
8	—	—	—	61.7	—	84.2	24	52.8*	—	—	292.3*
3.0	98.8	—	—	59.6	—	79.5	18	40.6*	—	—	282.5*
2	96.5	—	—	57.2	—	75.3	13	29.4*	—	—	274.8*
4	93.6	—	—	54.2	—	71.5	8.5	19.8*	—	—	268.5*
6	90.5	—	—	51.6	—	67.8	—	11.9*	—	—	263.3*
8	86.8	—	—	48.0	—	64.5	—	5.3*	—	—	257.3*
4.0	82.5	—	—	44.0	—	61.5	—	—	0.8*	—	252.5*
2	77.7	—	—	39.2	—	58.6	—	—	7.4*	—	247.3*
4	73.5	—	—	—	—	55.9	—	—	15.0*	—	241.8*
6	70.0	—	—	—	—	51.8	—	—	24.3*	—	236.3*
8	66.0	—	—	—	—	50.7	—	—	35.4*	9	231.1*
5.0	62.5	—	—	—	4.0	48.5	—	—	47.7*	—	225.9*
2	60.0	—	—	—	15.0	46.4	—	—	59.9*	—	220.3*
4	57.5	—	—	—	23.5	44.3	—	—	70.9*	3.1	214.7*
6	55.5	—	—	—	31.0	42.0	—	—	79.7*	5.0	209.0*
8	53.5	—	92.1	—	36.0	39.6	—	—	86.0*	8.0	203.1*
6.0	—	—	87.7	—	40.5	36.9	—	—	90.9*	12.0	197.1*
2	—	—	83.0	—	43.5	33.9	—	10	94.0*	18.5	190.5*
4	—	—	77.0	—	45.6	30.8	—	—	—	26.2	183.7*
6	—	—	71.2	—	—	27.3	—	—	—	36.0	176.8*
8	—	—	65.8	—	—	22.8	—	47.8	—	50.0	169.6*
7.0	—	—	61.0	—	—	17.7	—	46.4	—	61.0	163.3*
2	—	—	56.6	—	—	13.1	—	44.6	—	72.0	157.3*
4	—	—	53.6	—	—	9.2	—	41.9	—	80.8	151.8*
6	—	—	50.8	—	—	6.4	—	38.5	—	87.0	147.2*
8	—	5.22*	48.0	—	—	4.3	—	33.8	—	91.5	143.4*
8.0	—	7.94*	45.0	—	—	2.8	—	28.4	—	94.5	140.1*
2	—	11.80*	42.4	—	—	—	6b	23.1	—	—	137.3*
4	—	17.0*	38.0	—	—	—	—	17.7	—	—	134.5*
6	—	24.0*	32.0	—	—	—	—	12.9	—	—	130.5*
8	—	32.6*	24.8	—	—	—	pH	9.2	—	—	124.5*
9.0	—	42.6*	13.2	—	—	—	11.0	6.4	—	—	118.8*
2	—	53.4*	0.0	—	—	—	15.0	4.8	—	—	111.9*
4	—	64.0*	—	—	—	—	20.5	2.6	—	—	105.6*
6	—	73.7*	—	—	—	—	26.5	1.5	—	—	99.7*
8	—	81.6*	—	—	—	—	32.0	—	—	—	94.1*
10.0	—	87.8*	—	—	—	—	37.5	—	—	—	89.6*
2	—	—	—	—	—	—	41.0	—	—	—	84.9*
4	—	—	—	—	—	—	44.0	—	—	—	81.8*
6	—	—	—	—	—	—	46.0	—	—	—	79.8*
8	—	—	—	—	—	—	47.5	—	—	—	77.0*
							13.0	92.5			13.0

¹) Nos. 1-10 after KOLTHOFF, *Säure-Basen-Indikatoren*, Berlin, 1932; No. 11 after TEORELL and STENHAGEN, *Biochem. Z.*, 299, 416, 1938.

Based on data of the Swiss Federal Materials Testing and Research Institute, St.Gallen (Prof. Dr. A. ENGELER)



* GEIGY product.

Nitric acid

Spec. grav.	° Baumé (NBS scale)	Grams per litre	% HNO ₃	N	Spec. grav.	° Baumé (NBS scale)	Grams per litre	% HNO ₃	N	Spec. grav.	° Baumé (NBS scale)	Grams per litre	% HNO ₃	N
1.0036	0.5	10.04	1	0.159	1.2205	26.2	439.4	36	6.97	1.4176	42.7	1006	71	16.0
1.0091	1.3	20.18	2	0.320	1.2270	26.8	454.0	37	7.20	1.4218	43.0	1024	72	16.3
1.0146	2.1	30.44	3	0.483	1.2335	27.5	468.7	38	7.44	1.4258	43.3	1041	73	16.5
1.0201	2.9	40.80	4	0.647	1.2399	28.1	483.6	39	7.67	1.4298	43.6	1058	74	16.8
1.0256	3.6	51.28	5	0.814	1.2463	28.7	498.5	40	7.91	1.4337	43.9	1075	75	17.1
1.0312	4.4	61.87	6	0.982	1.2527	29.3	513.6	41	8.15	1.4375	44.1	1093	76	17.3
1.0369	5.2	72.58	7	1.15	1.2591	29.8	528.8	42	8.39	1.4413	44.4	1110	77	17.6
1.0427	5.9	83.42	8	1.32	1.2655	30.4	544.2	43	8.64	1.4450	44.7	1127	78	17.9
1.0485	6.7	94.37	9	1.50	1.2719	31.0	559.6	44	8.88	1.4486	44.9	1144	79	18.2
1.0543	7.5	105.4	10	1.67	1.2783	31.6	575.2	45	9.13	1.4521	45.1	1162	80	18.4
1.0602	8.2	116.6	11	1.85	1.2847	32.1	591.0	46	9.38	1.4555	45.4	1179	81	18.7
1.0661	9.0	127.9	12	2.03	1.2911	32.7	606.8	47	9.63	1.4589	45.6	1196	82	19.0
1.0721	9.8	139.4	13	2.21	1.2975	33.2	622.8	48	9.88	1.4622	45.8	1214	83	19.3
1.0781	10.5	150.9	14	2.39	1.3040	33.8	639.0	49	10.1	1.4655	46.1	1231	84	19.5
1.0842	11.3	162.6	15	2.58	1.3100	34.3	655.0	50	10.4	1.4686	46.3	1248	85	19.8
1.0903	12.0	174.4	16	2.77	1.3160	34.8	671.2	51	10.7	1.4716	46.5	1266	86	20.1
1.0964	12.8	186.4	17	2.96	1.3219	35.3	687.4	52	10.9	1.4745	46.7	1283	87	20.4
1.1026	13.5	198.5	18	3.15	1.3278	35.8	703.7	53	11.1	1.4773	46.8	1300	88	20.6
1.1088	14.2	210.7	19	3.34	1.3336	36.3	720.1	54	11.4	1.4800	47.0	1317	89	20.9
1.1150	15.0	223.0	20	3.54	1.3393	36.7	736.6	55	11.7	1.4826	47.2	1334	90	21.2
1.1213	15.7	235.5	21	3.74	1.3449	37.2	753.1	56	12.0	1.4850	47.4	1351	91	21.4
1.1276	16.4	248.1	22	3.94	1.3505	37.6	769.8	57	12.2	1.4873	47.5	1368	92	21.7
1.1340	17.1	260.8	23	4.13	1.3560	38.1	786.5	58	12.5	1.4892	47.6	1385	93	22.0
1.1404	17.9	273.7	24	4.34	1.3614	38.5	803.2	59	12.7	1.4912	47.8	1402	94	22.3
1.1469	18.6	286.7	25	4.55	1.3667	38.9	820.0	60	13.0	1.4932	47.9	1419	95	22.5
1.1534	19.4	299.9	26	4.76	1.3719	39.3	836.9	61	13.3	1.4952	48.0	1435	96	22.8
1.1600	20.0	313.2	27	4.97	1.3769	39.7	853.7	62	13.5	1.4974	48.2	1452	97	23.0
1.1666	20.7	326.6	28	5.18	1.3818	40.1	870.5	63	13.8	1.5008	48.4	1471	98	23.3
1.1733	21.4	340.3	29	5.40	1.3866	40.4	887.4	64	14.1	1.5056	48.7	1491	99	23.7
1.1800	22.1	354.0	30	5.62	1.3913	40.8	904.3	65	14.4	1.5129	49.2	1513	100	24.0
1.1867	22.8	367.9	31	5.84	1.3959	41.1	921.3	66	14.6					
1.1934	23.5	381.9	32	6.06	1.4004	41.5	938.3	67	14.9					
1.2002	24.2	396.1	33	6.29	1.4048	41.8	955.3	68	15.2					
1.2071	24.9	410.4	34	6.51	1.4091	42.1	972.3	69	15.4					
1.2140	25.6	424.9	35	6.74	1.4134	42.4	989.4	70	15.7					

Sulphuric acid

Spec. grav.	° Baumé (NBS scale)	Grams per litre	% H ₂ SO ₄	N	Spec. grav.	° Baumé (NBS scale)	Grams per litre	% H ₂ SO ₄	N	Spec. grav.	° Baumé (NBS scale)	Grams per litre	% H ₂ SO ₄	N
1.0051	0.7	10.05	1	0.205	1.2684	30.7	456.6	36	9.31	1.6221	55.6	1152	71	23.5
1.0118	1.7	20.24	2	0.413	1.2769	31.4	472.5	37	9.64	1.6338	56.3	1176	72	24.0
1.0184	2.6	30.55	3	0.623	1.2855	32.2	488.5	38	9.96	1.6456	56.9	1201	73	24.5
1.0250	3.5	41.00	4	0.836	1.2941	33.0	504.7	39	10.3	1.6574	57.5	1226	74	25.0
1.0317	4.5	51.59	5	1.05	1.3028	33.7	521.1	40	10.6	1.6692	58.1	1252	75	25.5
1.0385	5.4	62.31	6	1.27	1.3116	34.5	537.8	41	11.0	1.6810	58.7	1278	76	26.1
1.0453	6.3	73.17	7	1.49	1.3205	35.2	554.6	42	11.3	1.6927	59.3	1303	77	26.6
1.0522	7.2	84.18	8	1.72	1.3294	35.9	571.6	43	11.7	1.7043	59.9	1329	78	27.1
1.0591	8.1	95.32	9	1.94	1.3384	36.7	588.9	44	12.0	1.7158	60.5	1355	79	27.6
1.0661	9.0	106.6	10	2.17	1.3476	37.4	606.4	45	12.4	1.7272	61.1	1382	80	28.2
1.0731	9.9	118.0	11	2.41	1.3569	38.1	624.2	46	12.7	1.7383	61.6	1408	81	28.7
1.0802	10.8	129.6	12	2.64	1.3663	38.9	642.2	47	13.1	1.7491	62.1	1434	82	29.2
1.0874	11.7	141.4	13	2.88	1.3758	39.6	660.4	48	13.5	1.7594	62.6	1460	83	29.8
1.0947	12.5	153.3	14	3.13	1.3854	40.3	678.8	49	13.8	1.7693	63.0	1486	84	30.3
1.1020	13.4	165.3	15	3.37	1.3951	41.1	697.6	50	14.2	1.7786	63.5	1512	85	30.8
1.1094	14.3	177.5	16	3.62	1.4049	41.8	716.5	51	14.6	1.7872	63.9	1537	86	31.3
1.1168	15.2	189.9	17	3.87	1.4148	42.5	735.7	52	15.0	1.7951	64.2	1562	87	31.9
1.1243	16.0	202.4	18	4.13	1.4248	43.2	755.1	53	15.4	1.8022	64.5	1586	88	32.3
1.1318	16.9	215.0	19	4.38	1.4350	44.0	774.9	54	15.8	1.8087	64.8	1610	89	32.8
1.1394	17.7	227.9	20	4.65	1.4453	44.7	794.9	55	16.2	1.8144	65.1	1633	90	33.3
1.1471	18.6	240.9	21	4.91	1.4557	45.4	815.2	56	16.6	1.8195	65.3	1656	91	33.8
1.1548	19.4	254.1	22	5.18	1.4662	46.1	835.7	57	17.0	1.8240	65.5	1678	92	34.2
1.1626	20.3	267.4	23	5.45	1.4768	46.8	856.5	58	17.5	1.8279	65.7	1700	93	34.7
1.1704	21.1	280.9	24	5.73	1.4875	47.5	877.6	59	17.9	1.8312	65.8	1721	94	35.1
1.1783	21.9	294.6	25	6.01	1.4983	48.2	899.0	60	18.3	1.8337	65.9	1742	95	35.5
1.1862	22.8	308.4	26	6.29	1.5091	48.9	920.6	61	18.8	1.8355	66.0	1762	96	35.9
1.1942	23.6	322.4	27	6.57	1.5200	49.6	942.4	62	19.2	1.8364	66.0	1781	97	36.3
1.2023	24.4	336.6	28	6.86	1.5310	50.3	964.5	63	19.7	1.8361	66.0	1799	98	36.7
1.2104	25.2	351.0	29	7.16	1.5421	51.0	986.9	64	20.1	1.8342	65.9	1816	99	37.0
1.2185	26.0	365.6	30	7.46	1.5533	51.7	1010	65	20.6	1.8305	65.8	1831	100	37.3
1.2267	26.8	380.3	31	7.76	1.5646	52.3	1033	66	21.1					
1.2349	27.6	395.2	32	8.06	1.5760	53.0	1056	67	21.5					
1.2432	28.4	410.3	33	8.37	1.5874	53.7	1079	68	22.0					
1.2515	29.1	425.5	34	8.68	1.5989	54.3	1103	69	22.5					
1.2599	29.9	441.0	35	8.99	1.6105	55.0	1127	70	23.0					

¹) Taken from LANGE, N. A., and FORKER, G. M., *Handbook of Chemistry*, Sandusky, 1949; and *Handbook of Chemistry and Physics*, Cleveland, 1954-55.

Acetic acid								Phosphoric acid					
Spec. grav.	° Baumé (NBS scale)	Grams per litre	% C ₂ H ₄ O ₂	Spec. grav.	° Baumé (NBS scale)	Grams per litre	% C ₂ H ₄ O ₂	Spec. grav.	° Baumé (NBS scale)	Grams per litre	% H ₃ PO ₄	Grams per litre	% P ₂ O ₅
0.9982	0	1.0575	7.9	528.8	50	1.0038	0.6	10.04	1	7.271	0.7244
0.9996	...	9.996	1	1.0582	8.0	539.7	51	1.0092	1.3	20.18	2	14.62	1.449
1.0012	0.2	20.02	2	1.0590	8.1	550.7	52	1.0200	2.8	40.80	4	29.56	2.898
1.0025	0.4	30.08	3	1.0597	8.2	561.6	53	1.0309	4.3	61.85	6	44.81	4.346
1.0040	0.6	40.16	4	1.0604	8.3	572.6	54	1.0420	5.8	83.36	8	60.39	5.795
1.0055	0.8	50.28	5	1.0611	8.4	583.6	55	1.0532	7.3	105.3	10	76.29	7.244
1.0069	1.0	60.41	6	1.0618	8.4	594.6	56	1.0647	8.8	127.8	12	92.55	8.693
1.0083	1.2	70.58	7	1.0624	8.5	605.6	57	1.0764	10.3	150.7	14	109.2	10.14
1.0097	1.4	80.78	8	1.0631	8.6	616.6	58	1.0884	11.8	174.1	16	126.1	11.59
1.0111	1.6	91.00	9	1.0637	8.7	627.6	59	1.1008	13.3	198.1	18	143.5	13.04
1.0125	1.8	101.3	10	1.0642	8.8	638.5	60	1.1134	14.8	222.7	20	161.3	14.49
1.0139	2.0	111.5	11	1.0648	8.8	649.5	61	1.1263	16.3	247.8	22	179.5	15.94
1.0154	2.2	121.8	12	1.0653	8.9	660.5	62	1.1395	17.8	273.5	24	198.1	17.39
1.0168	2.4	132.2	13	1.0658	9.0	671.5	63	1.1529	19.2	299.8	26	217.1	18.83
1.0182	2.6	142.5	14	1.0662	9.0	682.4	64	1.1665	20.7	326.6	28	236.6	20.28
1.0195	2.8	152.9	15	1.0666	9.1	693.3	65	1.1805	22.2	354.2	30	256.5	21.73
1.0209	3.0	163.3	16	1.0671	9.1	704.3	66	1.216	25.8	425.6	35	308.3	25.35
1.0223	3.2	173.8	17	1.0675	9.2	715.2	67	1.254	29.4	501.6	40	363.4	28.98
1.0236	3.3	184.2	18	1.0678	9.2	726.1	68	1.293	32.9	581.9	45	421.5	32.60
1.0250	3.5	194.8	19	1.0682	9.3	737.1	69	1.335	36.4	667.5	50	483.5	36.22
1.0263	3.7	205.3	20	1.0685	9.3	748.0	70	1.379	39.9	758.5	55	549.4	39.84
1.0276	3.9	215.8	21	1.0687	9.3	758.8	71	1.426	43.3	855.6	60	619.8	43.46
1.0288	4.1	226.3	22	1.0690	9.4	769.7	72	1.475	46.7	958.8	65	694.5	47.09
1.0301	4.2	236.9	23	1.0693	9.4	780.6	73	1.526	50.0	1068	70	773.8	50.71
1.0313	4.4	247.5	24	1.0694	9.4	791.4	74	1.579	53.2	1184	75	857.9	54.33
1.0326	4.6	258.2	25	1.0696	9.4	802.2	75	1.633	56.2	1306	80	946.4	57.95
1.0338	4.7	268.8	26	1.0698	9.5	813.0	76	1.689	59.2	1436	85	1040	61.57
1.0349	4.9	279.4	27	1.0699	9.5	823.8	77	1.746	62.0	1571	90	1138	65.20
1.0361	5.1	290.1	28	1.0700	9.5	834.6	78	1.770	63.1	1628	92	1180	66.64
1.0372	5.2	300.8	29	1.0700	9.5	845.3	79	1.794	64.2	1686	94	1222	68.09
1.0384	5.4	311.5	30	1.0700	9.5	856.0	80	1.819	65.3	1746	96	1265	69.54
1.0395	5.5	322.2	31	1.0699	9.5	866.6	81	1.844	66.4	1807	98	1309	70.99
1.0406	5.7	333.0	32	1.0698	9.5	877.2	82	1.870	67.5	1870	100	1355	72.44
1.0417	5.8	343.8	33	1.0696	9.4	887.8	83						
1.0428	6.0	354.6	34	1.0693	9.4	898.2	84						
1.0438	6.1	365.3	35	1.0689	9.4	908.6	85						
1.0449	6.2	376.2	36	1.0685	9.3	918.9	86						
1.0459	6.4	387.0	37	1.0680	9.2	929.2	87						
1.0469	6.5	397.8	38	1.0675	9.2	939.4	88						
1.0479	6.6	408.7	39	1.0668	9.1	949.5	89						
				1.0661	9.0	959.5	90						
1.0488	6.8	419.5	40	1.0652	8.9	969.3	91						
1.0498	6.9	430.4	41	1.0643	8.8	979.2	92						
1.0507	7.0	441.3	42	1.0632	8.6	988.8	93						
1.0516	7.1	452.2	43	1.0619	8.5	998.2	94						
1.0525	7.2	463.1	44	1.0605	8.3	1007	95						
1.0534	7.4	474.0	45	1.0588	8.1	1016	96						
1.0542	7.5	484.9	46	1.0570	7.8	1025	97						
1.0551	7.6	495.9	47	1.0549	7.6	1034	98						
1.0559	7.7	506.8	48	1.0524	7.2	1042	99						
1.0567	7.8	517.8	49	1.0498	6.9	1050	100						

Sodium thiosulphate					
Spec. grav.	° Baumé (NBS scale)	Grams per litre	% Na ₂ S ₂ O ₃	Grams per litre	% Na ₂ S ₂ O ₃ · 5H ₂ O
1.0065	0.9	10.07	1	15.80	1.570
1.0148	2.1	20.30	2	31.86	3.139
1.0315	4.4	41.26	4	64.77	6.279
1.0483	6.7	62.90	6	98.73	9.418
1.0654	8.9	85.23	8	133.8	12.56
1.0827	11.1	108.3	10	170.0	15.70
1.1003	13.2	132.0	12	207.3	18.84
1.1182	15.3	156.5	14	245.7	21.98
1.1365	17.4	181.8	16	285.4	25.12
1.1551	19.5	207.9	18	326.4	28.25
1.1740	21.5	234.8	20	368.6	31.39
1.1932	23.5	262.5	22	412.1	34.53
1.2128	25.4	291.1	24	456.9	37.67
1.2328	27.4	320.5	26	503.1	40.81
1.2532	29.3	350.9	28	550.8	43.95
1.2739	31.2	382.2	30	599.9	47.09
1.3273	35.8	464.6	35	729.2	54.94
1.3827	40.1	553.1	40	868.2	62.79

Hydrochloric acid				
Spec. grav.	° Baumé (NBS scale)	Grams per litre	% HCl	N
1.0032	0.5	10.03	1	0.275
1.0082	1.2	20.16	2	0.553
1.0181	2.6	40.72	4	1.12
1.0279	3.9	61.67	6	1.69
1.0376	5.3	83.01	8	2.28
1.0474	6.6	104.7	10	2.87
1.0574	7.9	126.9	12	3.48
1.0675	9.2	149.5	14	4.10
1.0776	10.4	172.4	16	4.73
1.0878	11.7	195.8	18	5.37
1.0980	12.9	219.6	20	6.02
1.1083	14.2	243.8	22	6.69
1.1187	15.4	268.5	24	7.36
1.1290	16.6	293.5	26	8.05
1.1392	17.7	319.0	28	8.75
1.1492	18.8	344.8	30	9.46
1.1593	19.9	371.0	32	10.2
1.1691	21.0	397.5	34	10.9
1.1789	22.0	424.4	36	11.6
1.1885	23.0	451.6	38	12.4
1.1980	24.0	479.2	40	13.1

Ferric chloride			
Spec. grav.	° Baumé (NBS scale)	Grams per litre	% FeCl ₃
1.007	1.0	10.07	1
1.015	2.1	20.30	2
1.032	4.5	41.28	4
1.049	6.8	62.94	6
1.067	9.1	85.36	8
1.085	11.4	108.5	10
1.104	13.7	132.5	12
1.123	15.9	157.2	14
1.142	18.0	182.7	16
1.162	20.2	209.2	18
1.182	22.3	236.4	20
1.234	27.5	308.5	25
1.291	32.7	387.3	30
1.353	37.8	473.6	35
1.418	42.7	567.2	40
1.485	47.4	668.3	45
1.551	51.5	775.5	50

¹) Taken from LANGE, N. A., and FORKER, G. M., *Handbook of Chemistry*, Sandusky, 1949; and *Handbook of Chemistry and Physics*, Cleveland, 1954-55.

Barium chloride						Calcium chloride					
Spec. grav.	° Baumé (NBS scale)	Grams per litre	% BaCl ₂	Grams per litre	% BaCl ₂ ·2H ₂ O	Spec. grav.	° Baumé (NBS scale)	Grams per litre	% CaCl ₂	Grams per litre	% CaCl ₂ ·6H ₂ O
1.0159	2.3	20.32	2	23.83	2.346	1.0148	2.1	20.30	2	40.06	3.948
1.0341	4.8	41.36	4	48.52	4.692	1.0316	4.4	41.26	4	81.46	7.896
1.0528	7.3	63.17	6	74.10	7.038	1.0486	6.7	62.92	6	124.2	11.84
1.0721	9.8	85.77	8	100.6	9.384	1.0659	9.0	85.27	8	168.3	15.79
1.0921	12.2	109.2	10	128.1	11.73	1.0835	11.2	108.4	10	213.9	19.74
1.1128	14.7	133.5	12	156.6	14.08	1.1015	13.4	132.2	12	260.9	23.69
1.1342	17.2	158.8	14	186.3	16.42	1.1198	15.5	156.8	14	309.5	27.64
1.1564	19.6	185.0	16	217.0	18.77	1.1386	17.7	182.2	16	359.6	31.58
1.1793	22.0	212.3	18	249.0	21.11	1.1578	19.8	208.4	18	411.4	35.53
1.2031	24.5	240.6	20	282.2	23.46	1.1775	21.9	235.5	20	465.9	39.48
1.2277	26.9	270.1	22	316.8	25.81	1.2284	27.0	307.1	25	606.2	49.35
1.2531	29.3	300.7	24	352.8	28.15	1.2816	31.9	384.5	30	759.0	59.22
1.2793	31.7	332.6	26	390.2	30.50	1.3373	36.6	468.1	35	923.9	69.09
						1.3957	41.1	558.3	40	1102.0	78.96

Sodium chloride				Sodium sulphate					
Spec. grav.	° Baumé (NBS scale)	Grams per litre	% NaCl	Spec. grav.	° Baumé (NBS scale)	Grams per litre	% Na ₂ SO ₄	Grams per litre	% Na ₂ SO ₄ ·10H ₂ O
1.0053	0.8	10.05	1	1.0073	1.1	10.07	1	22.85	2.268
1.0125	1.8	20.25	2	1.0164	2.3	20.33	2	46.11	4.536
1.0268	3.8	41.07	4	1.0348	4.9	41.39	4	93.88	9.073
1.0413	5.8	62.48	6	1.0535	7.4	63.21	6	143.4	13.61
1.0559	7.7	84.47	8	1.0724	9.8	85.79	8	194.6	18.15
1.0707	9.6	107.1	10	1.0915	12.2	109.2	10	247.6	22.68
1.0857	11.5	130.3	12	1.1109	14.5	133.3	12	302.4	27.22
1.1009	13.3	154.1	14	1.1306	16.8	158.3	14	359.0	31.75
1.1162	15.1	178.6	16	1.1506	19.0	184.1	16	417.6	36.29
1.1319	16.9	203.7	18	1.1709	21.2	210.8	18	478.1	40.83
1.1478	18.7	229.6	20	1.1915	23.3	238.3	20	540.5	45.36
1.1640	20.4	256.1	22	1.2124	25.4	266.7	22	605.0	49.90
1.1804	22.2	283.3	24	1.2336	27.5	296.1	24	671.5	54.44
1.1972	23.9	311.3	26						

Conversion of hydrometer scales

<div><div><div>m = value of 1 degree on the scale</div><div>ρ = density</div><div>T = standard temperature of the scale</div></div></div>				Density greater than 1								
Name	T °C	$\rho > 1$	$\rho < 1$	Densi- ty	° Baumé NBS scale	Twad- dell	Densi- ty	° Baumé NBS scale	Twad- dell	Densi- ty	° Baumé NBS scale	Twad- dell
Balling	17.5	$\rho = \frac{200}{200 - m}$	$\rho = \frac{200}{200 + m}$	1.00	0.00	0	1.35	37.59	70	1.70	59.71	140
				1.01	1.44	2	1.36	38.38	72	1.71	60.20	142
Baumé (rational) (Germany)	15	$\rho = \frac{144.3}{144.3 - m}$	$\rho = \frac{144.3}{144.3 + m}$	1.02	2.84	4	1.37	39.16	74	1.72	60.70	144
				1.03	4.22	6	1.38	39.93	76	1.73	61.18	146
Baumé (National Bureau of Standards) ² (America)	15.56 (60°F)	$\rho = \frac{145}{145 - m}$	$\rho = \frac{140}{130 + m}$	1.04	5.58	8	1.39	40.68	78	1.74	61.67	148
				1.05	6.91	10	1.40	41.43	80	1.75	62.14	150
Baumé (Holland)	12.5	$\rho = \frac{144}{144 - m}$	$\rho = \frac{144}{145 + m}$	1.06	8.21	12	1.41	42.16	82	1.76	62.61	152
				1.07	9.49	14	1.42	42.89	84	1.77	63.08	154
Baumé (Gerlach)	17.5	$\rho = \frac{146.3}{146.3 - m}$	$\rho = \frac{146.3}{146.3 + m}$	1.08	10.74	16	1.43	43.60	86	1.78	63.54	156
				1.09	11.97	18	1.44	44.31	88	1.79	63.99	158
Beck	12.5	$\rho = \frac{170}{170 - m}$	$\rho = \frac{170}{170 + m}$	1.10	13.18	20	1.45	45.00	90	1.80	64.44	160
				1.11	14.37	22	1.46	45.68	92	1.81	64.89	162
Brix	15.625	$\rho = \frac{400}{400 - m}$	$\rho = \frac{400}{400 + m}$	1.12	15.54	24	1.47	46.36	94	1.82	65.31	164
				1.13	16.68	26	1.48	47.03	96	1.83	65.77	166
Cartier	12.5	$\rho = \frac{136.8}{126.1 - m}$	$\rho = \frac{136.8}{126.1 + m}$	1.14	17.81	28	1.49	47.68	98	1.84	66.20	168
				1.15	18.91	30	1.50	48.33	100	1.85	66.62	170
Stoppani	15.625	$\rho = \frac{166}{166 - m}$	$\rho = \frac{166}{166 + m}$	1.16	20.00	32	1.51	48.97	102	1.86	67.04	172
				1.17	21.07	34	1.52	49.60	104	1.87	67.46	174
Twaddell ³ (England)	15.56 (60°F)	$\rho = 1 + \frac{m}{200}$	not used	1.18	22.12	36	1.53	50.23	106	1.88	67.87	176
				1.19	23.15	38	1.54	50.84	108	1.89	68.28	178
				1.20	24.17	40	1.55	51.45	110	1.90	68.68	180
				1.21	25.16	42	1.56	52.05	112	1.91	69.08	182
				1.22	26.15	44	1.57	52.64	114	1.92	69.48	184
				1.23	27.11	46	1.58	53.23	116	1.93	69.87	186
				1.24	28.06	48	1.59	53.80	118	1.94	70.26	188
				1.25	29.00	50	1.60	54.38	120	1.95	70.64	190
				1.26	29.92	52	1.61	54.94	122	1.96	71.02	192
				1.27	30.83	54	1.62	55.49	124	1.97	71.40	194
				1.28	31.72	56	1.63	56.04	126	1.98	71.77	196
				1.29	32.60	58	1.64	56.58	128	1.99	72.14	198
				1.30	33.46	60	1.65	57.12	130	2.00	72.50	200
				1.31	34.31	62	1.66	57.65	132			
				1.32	35.15	64	1.67	58.17	134			
				1.33	35.98	66	1.68	58.69	136			
				1.34	36.79	68	1.69	59.20	138			

¹) Taken from LANGE, N. A., and FORKER, G. M., *Handbook of Chemistry*, Sandusky, 1949; and *Handbook of Chemistry and Physics*, Cleveland, 1954-55.
²) See adjacent table (NBS scale). ³) See adjacent table.

Potassium hydroxide*								Sodium hydroxide			
Spec. grav.	° Baumé (NBS scale)	Grams per litre	% KOH	Spec. grav.	° Baumé (NBS scale)	Grams per litre	% KOH	Spec. grav.	° Baumé (NBS scale)	Grams per litre	% NaOH
1.0083	1.2	10.08	1	1.3549	38.0	487.8	36	1.0095	1.4	10.10	1
1.0175	2.5	20.35	2	1.3659	38.8	505.4	37	1.0207	2.9	20.41	2
1.0267	3.8	30.80	3	1.3769	39.7	523.2	38	1.0318	4.5	30.95	3
1.0359	5.0	41.44	4	1.3879	40.5	541.3	39	1.0428	6.0	41.71	4
1.0452	6.3	52.26	5	1.3991	41.4	559.6	40	1.0538	7.4	52.69	5
				1.4103	42.2	578.2	41	1.0648	8.8	63.89	6
1.0544	7.5	63.26	6	1.4215	43.0	597.0	42	1.0758	10.2	75.31	7
1.0637	8.7	74.46	7	1.4329	43.8	616.1	43	1.0869	11.6	86.95	8
1.0730	9.9	85.84	8	1.4443	44.6	635.5	44	1.0979	12.9	98.81	9
1.0824	11.0	97.42	9	1.4558	45.4	655.1	45	1.1089	14.2	110.9	10
1.0918	12.2	109.2	10	1.4673	46.2	675.0	46	1.1309	16.8	135.7	12
				1.4790	47.0	695.1	47	1.1530	19.2	161.4	14
1.1013	13.3	121.1	11	1.4907	47.7	715.5	48	1.1751	21.6	188.0	16
1.1108	14.5	133.3	12	1.5025	48.5	736.2	49				
1.1203	15.6	145.6	13	1.5143	49.2	757.2	50	1.1972	23.9	215.5	18
1.1299	16.7	158.2	14	1.5262	50.0	778.4	51	1.2191	26.1	243.8	20
1.1396	17.8	170.9	15	1.5382	50.7	799.9	52	1.2411	28.2	273.0	22
				Ammonia				1.2629	30.2	303.1	24
1.1493	18.8	183.9	16					1.2848	32.1	334.0	26
1.1590	19.9	197.0	17	Spec. grav.	° Baumé (NBS scale)	Grams per litre	% NH ₃	1.3064	34.0	365.8	28
1.1688	20.9	210.4	18	0.9939	10.9	9.939	1	1.3279	35.8	398.4	30
1.1786	22.0	223.9	19	0.9895	11.5	19.79	2	1.3490	37.5	431.7	32
1.1884	23.0	237.7	20	0.9811	12.7	39.24	4	1.3696	39.1	465.7	34
				0.9730	13.9	58.38	6	1.3900	40.7	500.4	36
1.1984	24.0	251.7	21	0.9651	15.1	77.21	8	1.4101	42.2	535.8	38
1.2083	25.0	265.8	22	0.9575	16.2	95.75	10	1.4300	43.6	572.0	40
1.2184	26.0	280.2	23	0.9501	17.3	114.0	12	1.4494	45.0	608.7	42
1.2285	27.0	294.8	24	0.9430	18.5	132.0	14	1.4685	46.3	646.1	44
1.2387	27.9	309.7	25	0.9362	19.5	149.8	16	1.4873	47.5	684.2	46
				0.9295	20.6	167.3	18	1.5065	48.8	723.1	48
1.2489	28.9	324.7	26	0.9229	21.7	184.6	20	1.5253	49.9	762.7	50
1.2592	29.8	340.0	27	0.9164	22.8	201.6	22				
1.2695	30.8	355.5	28	0.9101	23.8	218.4	24				
1.2800	31.7	371.2	29	0.9040	24.9	235.0	26				
1.2905	32.6	387.2	30	0.8980	25.9	251.4	28				
				0.8920	27.0	267.6	30				
1.3010	33.6	403.3	31					* Values for potassium hydroxide at $\frac{15^{\circ}}{4^{\circ}}C$.			
1.3117	34.5	419.7	32								
1.3224	35.4	436.4	33								
1.3331	36.2	453.3	34								
1.3440	37.1	470.4	35								

Cane sugar (sucrose)											
Spec. grav.	° Baumé (NBS scale)	Grams per litre	% C ₁₂ H ₂₂ O ₁₁	Spec. grav.	° Baumé (NBS scale)	Grams per litre	% C ₁₂ H ₂₂ O ₁₁	Spec. grav.	° Baumé (NBS scale)	Grams per litre	% C ₁₂ H ₂₂ O ₁₁
0.9982	0	1.1270	16.3	338.1	30	1.2865	32.3	771.9	60
1.0021	0.3	10.02	1	1.1318	16.9	350.8	31	1.2924	32.8	788.3	61
1.0060	0.9	20.12	2	1.1366	17.5	363.7	32	1.2983	33.4	804.9	62
1.0099	1.4	30.30	3	1.1415	18.0	376.7	33	1.3043	33.9	821.7	63
1.0139	2.0	40.56	4	1.1463	18.6	389.8	34	1.3103	34.4	838.6	64
1.0179	2.5	50.89	5	1.1513	19.1	402.9	35	1.3163	34.8	855.6	65
1.0219	3.1	61.31	6	1.1562	19.6	416.2	36	1.3224	35.4	872.8	66
1.0259	3.6	71.81	7	1.1612	20.1	429.7	37	1.3286	35.9	890.1	67
1.0299	4.1	82.40	8	1.1663	20.7	443.2	38	1.3347	36.4	907.6	68
1.0340	4.7	93.06	9	1.1713	21.2	456.8	39	1.3409	36.9	925.2	69
1.0381	5.3	103.8	10	1.1764	21.7	470.6	40	1.3472	37.4	943.0	70
1.0423	5.8	114.7	11	1.1816	22.3	484.5	41	1.3535	37.9	961.0	71
1.0465	6.4	125.6	12	1.1868	22.8	498.4	42	1.3598	38.4	979.0	72
1.0507	7.0	136.6	13	1.1920	23.3	512.6	43	1.3661	38.9	997.3	73
1.0549	7.5	147.7	14	1.1972	23.9	526.8	44	1.3725	39.4	1016	74
1.0592	8.1	158.9	15	1.2025	24.4	541.1	45	1.3790	39.9	1034	75
1.0635	8.7	170.2	16	1.2079	25.0	555.6	46	1.3854	40.4	1053	76
1.0678	9.2	181.5	17	1.2132	25.5	570.2	47	1.3920	40.9	1072	77
1.0721	9.8	193.0	18	1.2186	26.0	584.9	48	1.3985	41.4	1091	78
1.0765	10.3	204.5	19	1.2241	26.5	599.8	49	1.4051	41.8	1110	79
1.0810	10.8	216.2	20	1.2296	27.1	614.8	50	1.4117	42.2	1129	80
1.0854	11.4	227.9	21	1.2351	27.6	629.9	51	1.4184	42.7	1149	81
1.0899	12.0	239.8	22	1.2406	28.1	645.1	52	1.4251	43.2	1169	82
1.0944	12.5	251.7	23	1.2462	28.7	660.5	53	1.4318	43.7	1188	83
1.0990	13.1	263.8	24	1.2519	29.2	676.0	54	1.4386	44.2	1208	84
1.1036	13.6	275.9	25	1.2575	29.7	691.6	55	1.4454	44.7	1229	85
1.1082	14.2	288.1	26	1.2632	30.3	707.4	56	1.4522	45.2	1249	86
1.1128	14.7	300.5	27	1.2690	30.8	723.3	57	1.4591	45.6	1269	87
1.1175	15.3	312.9	28	1.2748	31.3	739.4	58	1.4660	46.1	1290	88
1.1222	15.8	325.4	29	1.2806	31.8	755.6	59	1.4730	46.6	1311	89

1) Taken from LANGE, N. A., and FORKER, G. M., *Handbook of Chemistry*, Sandusky, 1949; and *Handbook of Chemistry and Physics*, Cleveland, 1954-55.

Glycerol $\left(\frac{20^{\circ}}{4^{\circ}}\text{C}\right)$											
Spec. grav.	° Baumé	Grams per litre	% $\text{C}_3\text{H}_8\text{O}_3$	Spec. grav.	° Baumé	Grams per litre	% $\text{C}_3\text{H}_8\text{O}_3$	Spec. grav.	° Baumé	Grams per litre	% $\text{C}_3\text{H}_8\text{O}_3$
1.00060	0.1	10.01	1	1.08600	11.5	380.1	35	1.18125	22.2	826.6	70
1.00300	0.4	20.06	2	1.08865	11.8	391.9	36	1.18395	22.5	840.4	71
1.00540	0.8	30.16	3	1.09135	12.1	403.8	37	1.18670	22.8	854.1	72
1.00780	1.1	40.31	4	1.09400	12.5	415.8	38	1.18940	23.1	868.0	73
1.01015	1.5	50.51	5	1.09665	12.8	427.8	39	1.19215	23.3	881.9	74
1.01255	1.8	60.75	6	1.09930	13.1	439.8	40	1.19485	23.6	895.8	75
1.01495	2.1	71.04	7	1.10200	13.4	451.9	41	1.19760	23.9	909.8	76
1.01730	2.5	81.38	8	1.10470	13.8	464.1	42	1.20030	24.2	923.8	77
1.01970	2.8	91.77	9	1.10740	14.1	476.2	43	1.20305	24.4	938.0	78
1.02210	3.1	102.2	10	1.11010	14.4	488.5	44	1.20575	24.7	952.1	79
1.02455	3.5	112.7	11	1.11280	14.7	500.8	45	1.20850	25.0	966.3	80
1.02705	3.8	123.3	12	1.11550	15.0	513.1	46	1.21115	25.2	980.6	81
1.02955	4.1	133.8	13	1.11820	15.3	525.6	47	1.21380	25.5	994.9	82
1.03200	4.5	144.5	14	1.12090	15.6	538.0	48	1.21650	25.8	1009	83
1.03450	4.8	155.2	15	1.12360	16.0	550.6	49	1.21915	26.0	1024	84
1.03695	5.2	165.9	16	1.12630	16.3	563.2	50	1.22180	26.3	1038	85
1.03945	5.5	176.7	17	1.12905	16.6	575.8	51	1.22445	26.5	1053	86
1.04195	5.8	187.6	18	1.13180	16.9	588.5	52	1.22710	26.8	1067	87
1.04440	6.2	198.5	19	1.13455	17.2	601.2	53	1.22975	27.1	1082	88
1.04690	6.5	209.4	20	1.13730	17.5	614.0	54	1.23245	27.3	1096	89
1.04950	6.8	220.4	21	1.14005	17.8	626.9	55	1.23510	27.6	1111	90
1.05205	7.2	231.4	22	1.14280	18.1	639.8	56	1.23770	27.8	1126	91
1.05465	7.5	242.5	23	1.14555	18.4	652.8	57	1.24035	28.1	1141	92
1.05720	7.8	253.7	24	1.14830	18.7	665.8	58	1.24300	28.3	1156	93
1.05980	8.2	264.9	25	1.15105	19.0	678.9	59	1.24560	28.6	1171	94
1.06240	8.5	276.2	26	1.15380	19.3	692.0	60	1.24825	28.8	1186	95
1.06495	8.8	287.5	27	1.15655	19.6	705.2	61	1.25080	29.1	1201	96
1.06755	9.2	298.9	28	1.15930	19.9	718.4	62	1.25335	29.3	1216	97
1.07010	9.5	310.3	29	1.16205	20.2	731.7	63	1.25590	29.5	1231	98
1.07270	9.8	321.8	30	1.16475	20.5	745.1	64	1.25850	29.8	1246	99
1.07535	10.2	333.3	31	1.16750	20.8	758.6	65	1.26108	30.0	1261	100
1.07800	10.5	345.0	32	1.17025	21.0	772.0	66				
1.08070	10.8	356.6	33	1.17300	21.3	785.5	67				
1.08335	11.2	368.3	34	1.17575	21.6	799.1	68				
				1.17850	21.9	812.8	69				

Ethyl alcohol $\left(\frac{15.56^{\circ}}{15.56^{\circ}}\text{C}\right)$											
Spec. grav.	Vol%	Wt.%	g/100 ml	Spec. grav.	Vol%	Wt.%	g/100 ml	Spec. grav.	Vol%	Wt.%	g/100 ml
1.00000	0.00	0.00	0.00	0.99487	3.50	2.80	2.78	0.99021	7.00	5.61	5.56
0.99984	0.10	0.08	0.08	0.99473	3.60	2.88	2.86	0.99009	7.10	5.69	5.64
0.99968	0.20	0.16	0.16	0.99459	3.70	2.96	2.94	0.98996	7.20	5.77	5.72
0.99953	0.30	0.24	0.24	0.99445	3.80	3.04	3.02	0.98984	7.30	5.86	5.80
0.99937	0.40	0.32	0.32	0.99431	3.90	3.12	3.10	0.98971	7.40	5.94	5.88
0.99923	0.50	0.40	0.40	0.99417	4.00	3.20	3.18	0.98959	7.50	6.02	5.96
0.99907	0.60	0.48	0.48	0.99403	4.10	3.28	3.26	0.98947	7.60	6.10	6.04
0.99892	0.70	0.56	0.56	0.99390	4.20	3.36	3.34	0.98934	7.70	6.18	6.11
0.99877	0.80	0.64	0.64	0.99376	4.30	3.44	3.42	0.98922	7.80	6.26	6.19
0.99861	0.90	0.71	0.71	0.99363	4.40	3.52	3.50	0.98909	7.90	6.34	6.27
0.99849	1.00	0.79	0.79	0.99349	4.50	3.60	3.58	0.98897	8.00	6.42	6.35
0.99834	1.10	0.87	0.87	0.99335	4.60	3.68	3.66	0.98885	8.10	6.50	6.43
0.99819	1.20	0.95	0.95	0.99322	4.70	3.76	3.74	0.98873	8.20	6.58	6.51
0.99805	1.30	1.03	1.03	0.99308	4.80	3.84	3.81	0.98861	8.30	6.67	6.59
0.99790	1.40	1.11	1.11	0.99295	4.90	3.92	3.89	0.98849	8.40	6.75	6.67
0.99775	1.50	1.19	1.19	0.99281	5.00	4.00	3.97	0.98837	8.50	6.83	6.75
0.99760	1.60	1.27	1.27	0.99268	5.10	4.08	4.05	0.98825	8.60	6.91	6.83
0.99745	1.70	1.35	1.35	0.99255	5.20	4.16	4.13	0.98813	8.70	6.99	6.91
0.99731	1.80	1.43	1.43	0.99241	5.30	4.24	4.21	0.98801	8.80	7.07	6.99
0.99716	1.90	1.51	1.51	0.99228	5.40	4.32	4.29	0.98789	8.90	7.15	7.07
0.99701	2.00	1.59	1.59	0.99215	5.50	4.40	4.37	0.98777	9.00	7.23	7.14
0.99687	2.10	1.67	1.66	0.99202	5.60	4.48	4.44	0.98765	9.10	7.31	7.22
0.99672	2.20	1.75	1.74	0.99189	5.70	4.56	4.52	0.98754	9.20	7.39	7.30
0.99658	2.30	1.83	1.82	0.99175	5.80	4.64	4.60	0.98742	9.30	7.48	7.38
0.99643	2.40	1.91	1.90	0.99162	5.90	4.72	4.68	0.98730	9.40	7.56	7.46
0.99629	2.50	1.99	1.98	0.99149	6.00	4.80	4.76	0.98719	9.50	7.64	7.54
0.99615	2.60	2.07	2.06	0.99136	6.10	4.88	4.84	0.98707	9.60	7.72	7.62
0.99600	2.70	2.15	2.14	0.99123	6.20	4.96	4.92	0.98695	9.70	7.80	7.70
0.99586	2.80	2.23	2.22	0.99111	6.30	5.05	5.00	0.98683	9.80	7.88	7.78
0.99571	2.90	2.31	2.30	0.99098	6.40	5.13	5.08	0.98672	9.90	7.96	7.85
0.99557	3.00	2.39	2.38	0.99085	6.50	5.21	5.16	0.98660	10.00	8.04	7.93
0.99543	3.10	2.47	2.46	0.99072	6.60	5.29	5.24	0.98649	10.10	8.12	8.01
0.99529	3.20	2.55	2.54	0.99059	6.70	5.37	5.32	0.98637	10.20	8.20	8.09
0.99515	3.30	2.64	2.62	0.99047	6.80	5.45	5.40	0.98626	10.30	8.29	8.17
0.99501	3.40	2.72	2.70	0.99034	6.90	5.53	5.48	0.98614	10.40	8.37	8.25

¹) Taken from LANGE, N. A., and FORKER, G. M., *Handbook of Chemistry*, Sandusky, 1949; and *Handbook of Chemistry and Physics*, Cleveland, 1954-55.

Ethyl alcohol $\left(\frac{15.56^\circ}{15.56^\circ} \text{C} \right)$ (continued)

Spec. grav.	Vol%	Wt. %	g/100 ml	Spec. grav.	Vol%	Wt. %	g/100 ml	Spec. grav.	Vol%	Wt. %	g/100 ml
0.98603	10.50	8.45	8.33	0.97808	18.00	14.60	14.28	0.97044	25.50	20.85	20.24
0.98592	10.60	8.53	8.41	0.97798	18.10	14.68	14.36	0.97033	25.60	20.93	20.32
0.98580	10.70	8.61	8.49	0.97788	18.20	14.77	14.44	0.97023	25.70	21.02	20.40
0.98569	10.80	8.70	8.57	0.97778	18.30	14.85	14.52	0.97012	25.80	21.10	20.47
0.98557	10.90	8.78	8.65	0.97768	18.40	14.94	14.60	0.97001	25.90	21.19	20.55
0.98546	11.00	8.86	8.73	0.97758	18.50	15.02	14.68	0.96991	26.00	21.27	20.63
0.98535	11.10	8.94	8.81	0.97748	18.60	15.10	14.76	0.96980	26.10	21.35	20.71
0.98524	11.20	9.02	8.89	0.97738	18.70	15.18	14.84	0.96969	26.20	21.44	20.79
0.98513	11.30	9.11	8.97	0.97728	18.80	15.27	14.92	0.96959	26.30	21.52	20.87
0.98502	11.40	9.19	9.05	0.97718	18.90	15.38	15.00	0.96949	26.40	21.61	20.95
0.98491	11.50	9.27	9.13	0.97708	19.00	15.43	15.08	0.96937	26.50	21.69	21.03
0.98479	11.60	9.35	9.21	0.97698	19.10	15.51	15.15	0.96926	26.60	21.77	21.11
0.98468	11.70	9.43	9.29	0.97688	19.20	15.59	15.23	0.96915	26.70	21.86	21.19
0.98457	11.80	9.51	9.36	0.97678	19.30	15.68	15.31	0.96905	26.80	21.94	21.27
0.98446	11.90	9.59	9.44	0.97668	19.40	15.76	15.39	0.96894	26.90	22.03	21.35
0.98435	12.00	9.67	9.52	0.97658	19.50	15.84	15.47	0.96883	27.00	22.11	21.43
0.98424	12.10	9.75	9.60	0.97648	19.60	15.93	15.55	0.96872	27.10	22.20	21.51
0.98413	12.20	9.83	9.68	0.97638	19.70	16.01	15.63	0.96861	27.20	22.28	21.59
0.98402	12.30	9.92	9.76	0.97628	19.80	16.09	15.71	0.96850	27.30	22.37	21.67
0.98391	12.40	10.00	9.84	0.97618	19.90	16.18	15.79	0.96839	27.40	22.45	21.75
0.98381	12.50	10.08	9.92	0.97608	20.00	16.26	15.87	0.96828	27.50	22.54	21.83
0.98370	12.60	10.16	10.00	0.97598	20.10	16.34	15.95	0.96816	27.60	22.62	21.90
0.98359	12.70	10.24	10.07	0.97588	20.20	16.42	16.03	0.96805	27.70	22.71	21.98
0.98348	12.80	10.33	10.15	0.97578	20.30	16.51	16.10	0.96794	27.80	22.79	22.06
0.98337	12.90	10.41	10.23	0.97568	20.40	16.59	16.18	0.96783	27.90	22.88	22.14
0.98326	13.00	10.49	10.31	0.97558	20.50	16.67	16.26	0.96772	28.00	22.96	22.22
0.98315	13.10	10.57	10.39	0.97547	20.60	16.75	16.34	0.96761	28.10	23.04	22.30
0.98305	13.20	10.65	10.47	0.97537	20.70	16.84	16.42	0.96749	28.20	23.13	22.38
0.98294	13.30	10.74	10.55	0.97527	20.80	16.92	16.50	0.96738	28.30	23.21	22.45
0.98283	13.40	10.82	10.63	0.97517	20.90	17.01	16.58	0.96726	28.40	23.30	22.53
0.98273	13.50	10.90	10.71	0.97507	21.00	17.09	16.66	0.96715	28.50	23.38	22.61
0.98262	13.60	10.98	10.79	0.97497	21.10	17.17	16.74	0.96704	28.60	23.47	22.69
0.98251	13.70	11.06	10.87	0.97487	21.20	17.26	16.82	0.96692	28.70	23.55	22.77
0.98240	13.80	11.15	10.95	0.97477	21.30	17.34	16.90	0.96681	28.80	23.64	22.85
0.98230	13.90	11.23	11.03	0.97467	21.40	17.43	16.98	0.96669	28.90	23.72	22.93
0.98219	14.00	11.31	11.11	0.97457	21.50	17.51	17.06	0.96658	29.00	23.81	23.01
0.98209	14.10	11.39	11.19	0.97446	21.60	17.59	17.14	0.96646	29.10	23.89	23.09
0.98198	14.20	11.47	11.27	0.97436	21.70	17.67	17.22	0.96635	29.20	23.98	23.17
0.98188	14.30	11.56	11.35	0.97426	21.80	17.76	17.30	0.96623	29.30	24.06	23.25
0.98177	14.40	11.64	11.43	0.97416	21.90	17.84	17.38	0.96611	29.40	24.15	23.33
0.98167	14.50	11.72	11.51	0.97406	22.00	17.92	17.46	0.96600	29.50	24.23	23.41
0.98156	14.60	11.80	11.59	0.97396	22.10	18.00	17.54	0.96587	29.60	24.32	23.49
0.98146	14.70	11.88	11.67	0.97386	22.20	18.09	17.62	0.96576	29.70	24.40	23.57
0.98135	14.80	11.97	11.75	0.97375	22.30	18.17	17.70	0.96564	29.80	24.49	23.65
0.98125	14.90	12.05	11.82	0.97365	22.40	18.26	17.78	0.96553	29.90	24.57	23.73
0.98114	15.00	12.13	11.90	0.97355	22.50	18.34	17.86	0.96541	30.00	24.66	23.81
0.98104	15.10	12.21	11.98	0.97345	22.60	18.42	17.94	0.96529	30.10	24.74	23.89
0.98093	15.20	12.29	12.06	0.97335	22.70	18.51	18.02	0.96517	30.20	24.83	23.97
0.98083	15.30	12.38	12.14	0.97324	22.80	18.59	18.10	0.96505	30.30	24.91	24.04
0.98073	15.40	12.46	12.22	0.97314	22.90	18.68	18.18	0.96493	30.40	25.00	24.12
0.98063	15.50	12.54	12.30	0.97304	23.00	18.76	18.26	0.96481	30.50	25.08	24.20
0.98052	15.60	12.62	12.37	0.97294	23.10	18.84	18.33	0.96469	30.60	25.17	24.28
0.98042	15.70	12.70	12.45	0.97283	23.20	18.92	18.41	0.96457	30.70	25.25	24.36
0.98032	15.80	12.79	12.53	0.97273	23.30	19.01	18.49	0.96445	30.80	25.34	24.44
0.98021	15.90	12.87	12.61	0.97263	23.40	19.09	18.57	0.96433	30.90	25.42	24.52
0.98011	16.00	12.95	12.69	0.97253	23.50	19.17	18.65	0.96421	31.00	25.51	24.60
0.98001	16.10	13.03	12.77	0.97242	23.60	19.25	18.73	0.96409	31.10	25.60	24.68
0.97991	16.20	13.12	12.85	0.97232	23.70	19.34	18.81	0.96396	31.20	25.68	24.76
0.97980	16.30	13.20	12.93	0.97222	23.80	19.42	18.88	0.96384	31.30	25.77	24.84
0.97970	16.40	13.29	13.01	0.97211	23.90	19.51	18.96	0.96372	31.40	25.85	24.92
0.97960	16.50	13.37	13.09	0.97201	24.00	19.59	19.04	0.96360	31.50	25.94	25.00
0.97950	16.60	13.45	13.17	0.97191	24.10	19.67	19.12	0.96347	31.60	26.03	25.08
0.97940	16.70	13.53	13.25	0.97180	24.20	19.76	19.20	0.96335	31.70	26.11	25.16
0.97929	16.80	13.62	13.33	0.97170	24.30	19.84	19.28	0.96323	31.80	26.20	25.24
0.97917	16.90	13.70	13.41	0.97159	24.40	19.93	19.36	0.96310	31.90	26.28	25.32
0.97909	17.00	13.78	13.49	0.97149	24.50	20.01	19.44	0.96298	32.00	26.37	25.40
0.97899	17.10	13.86	13.57	0.97139	24.60	20.09	19.52	0.96285	32.10	26.46	25.48
0.97889	17.20	13.94	13.65	0.97128	24.70	20.18	19.60	0.96273	32.20	26.54	25.56
0.97879	17.30	14.03	13.73	0.97118	24.80	20.26	19.68	0.96260	32.30	26.63	25.64
0.97869	17.40	14.11	13.81	0.97107	24.90	20.35	19.76	0.96248	32.40	26.71	25.71
0.97859	17.50	14.19	13.89	0.97097	25.00	20.43	19.84	0.96235	32.50	26.80	25.79
0.97848	17.60	14.27	13.96	0.97086	25.10	20.51	19.92	0.96222	32.60	26.89	25.87
0.97838	17.70	14.35	14.04	0.97076	25.20	20.60	20.00	0.96210	32.70	26.97	25.95
0.97828	17.80	14.44	14.12	0.97065	25.30	20.68	20.08	0.96197	32.80	27.06	26.03
0.97818	17.90	14.52	14.20	0.97055	25.40	20.77	20.16	0.96185	32.90	27.14	26.11

¹) Taken from LANGE, N. A., and FORKER, G. M., *Handbook of Chemistry*, Sandusky, 1949; and *Handbook of Chemistry and Physics*, Cleveland, 1954-55.

Ethyl alcohol $\left(\begin{smallmatrix} 15.56^{\circ} \\ 15.56^{\circ} \end{smallmatrix} \text{C} \right)$ (concluded)

Spec. grav.	Vol%	Wt. %	g/100 ml	Spec. grav.	Vol%	Wt. %	g/100 ml	Spec. grav.	Vol%	Wt. %	g/100 ml
0.96172	33.00	27.23	26.19	0.95107	40.50	33.79	32.14	0.93824	48.00	40.60	38.09
0.96159	33.10	27.32	26.27	0.95091	40.60	33.88	32.22	0.93805	48.10	40.69	38.17
0.96146	33.20	27.40	26.35	0.95075	40.70	33.97	32.30	0.93786	48.20	40.78	38.25
0.96133	33.30	27.49	26.43	0.95059	40.80	34.06	32.38	0.93768	48.30	40.88	38.33
0.96120	33.40	27.57	26.51	0.95044	40.90	34.15	32.46	0.93749	48.40	40.97	38.41
0.96108	33.50	27.66	26.59	0.95028	41.00	34.24	32.54	0.93730	48.50	41.06	38.49
0.96095	33.60	27.75	26.67	0.95012	41.10	34.33	32.62	0.93711	48.60	41.15	38.57
0.96082	33.70	27.83	26.75	0.94996	41.20	34.42	32.70	0.93692	48.70	41.24	38.65
0.96069	33.80	27.92	26.82	0.94980	41.30	34.50	32.78	0.93679	48.80	41.34	38.72
0.96056	33.90	28.00	26.90	0.94964	41.40	34.59	32.86	0.93655	48.90	41.43	38.80
0.96043	34.00	28.09	26.98	0.94948	41.50	34.68	32.93	0.93636	49.00	41.52	38.88
0.96030	34.10	28.18	27.06	0.94932	41.60	34.77	33.01	0.93617	49.10	41.61	38.96
0.96016	34.20	28.26	27.14	0.94916	41.70	34.86	33.09	0.93598	49.20	41.71	39.04
0.96003	34.30	28.35	27.22	0.94900	41.80	34.95	33.17	0.93578	49.30	41.80	39.12
0.95990	34.40	28.43	27.30	0.94884	41.90	35.04	33.25	0.93559	49.40	41.90	39.20
0.95977	34.50	28.52	27.38	0.94868	42.00	35.13	33.33	0.93540	49.50	41.99	39.28
0.95963	34.60	28.61	27.46	0.94852	42.10	35.22	33.41	0.93521	49.60	42.08	39.36
0.95950	34.70	28.70	27.54	0.94835	42.20	35.31	33.49	0.93502	49.70	42.18	39.44
0.95937	34.80	28.78	27.62	0.94810	42.30	35.40	33.57	0.93482	49.80	42.27	39.52
0.95923	34.90	28.87	27.70	0.94802	42.40	35.49	33.65	0.93463	49.90	42.37	39.60
0.95910	35.00	28.96	27.78	0.94786	42.50	35.58	33.73	0.9344	50.00	42.47	39.69
0.95896	35.10	29.05	27.86	0.94770	42.60	35.67	33.81	0.9325	51.00	43.41	40.48
0.95883	35.20	29.13	27.94	0.94753	42.70	35.76	33.89	0.9305	52.00	44.35	41.27
0.95869	35.30	29.22	28.02	0.94737	42.80	35.85	33.97	0.9285	53.00	45.31	42.07
0.95855	35.40	29.30	28.09	0.94720	42.90	35.94	34.04	0.9264	54.00	46.27	42.86
0.95842	35.50	29.38	28.17	0.94704	43.00	36.03	34.12	0.9244	55.00	47.23	43.66
0.95828	35.60	29.48	28.25	0.94687	43.10	36.12	34.20	0.9222	56.00	48.20	44.45
0.95814	35.70	29.57	28.33	0.94670	43.20	36.21	34.28	0.9201	57.00	49.18	45.23
0.95800	35.80	29.65	28.41	0.94654	43.30	36.30	34.36	0.9180	58.00	50.16	46.04
0.95787	35.90	29.74	28.49	0.94637	43.40	36.39	34.44	0.9158	59.00	51.15	46.83
0.95773	36.00	29.83	28.57	0.94620	43.50	36.48	34.52	0.9136	60.00	52.16	47.63
0.95759	36.10	29.92	28.65	0.94603	43.60	36.57	34.60	0.9113	61.00	53.15	48.41
0.95745	36.20	30.00	28.73	0.94586	43.70	36.66	34.68	0.9091	62.00	54.16	49.21
0.95731	36.30	30.09	28.81	0.94570	43.80	36.75	34.76	0.9068	63.00	55.16	50.00
0.95717	36.40	30.17	28.88	0.94553	43.90	36.84	34.84	0.9044	64.00	56.18	50.80
0.95703	36.50	30.26	28.96	0.94536	44.00	36.93	34.91	0.9021	65.00	57.21	51.59
0.95688	36.60	30.35	29.04	0.94519	44.10	37.02	34.99	0.8997	66.00	58.24	52.39
0.95674	36.70	30.44	29.12	0.94502	44.20	37.11	35.07	0.8974	67.00	59.28	53.19
0.95660	36.80	30.52	29.20	0.94484	44.30	37.21	35.15	0.8949	68.00	60.33	53.98
0.95646	36.90	30.61	29.29	0.94467	44.40	37.30	35.23	0.8925	69.00	61.39	54.77
0.95632	37.00	30.70	29.36	0.94450	44.50	37.39	35.31	0.8900	70.00	62.45	55.56
0.95618	37.10	30.79	29.44	0.94433	44.60	37.48	35.39	0.8876	71.00	63.51	56.36
0.95603	37.20	30.88	29.52	0.94416	44.70	37.57	35.47	0.8850	72.00	64.59	57.16
0.95589	37.30	30.96	29.60	0.94398	44.80	37.66	35.55	0.8825	73.00	65.67	57.95
0.95574	37.40	31.05	29.68	0.94381	44.90	37.76	35.63	0.8799	74.00	66.76	58.74
0.95560	37.50	31.14	29.76	0.94364	45.00	37.84	35.71	0.8773	75.00	67.84	59.53
0.95545	37.60	31.23	29.84	0.94346	45.10	37.93	35.79	0.8747	76.00	68.99	60.33
0.95531	37.70	31.32	29.92	0.94329	45.20	38.02	35.87	0.8721	77.00	70.10	61.12
0.95516	37.80	31.40	30.00	0.94311	45.30	38.12	35.95	0.8694	78.00	71.25	61.91
0.95502	37.90	31.49	30.08	0.94294	45.40	38.21	36.03	0.8667	79.00	72.38	62.71
0.95487	38.00	31.58	30.16	0.94276	45.50	38.30	36.11	0.8639	80.00	73.54	63.51
0.95472	38.10	31.67	30.24	0.94258	45.60	38.39	36.19	0.8611	81.00	74.68	64.30
0.95457	38.20	31.76	30.32	0.94241	45.70	38.48	36.26	0.8583	82.00	75.82	65.09
0.95442	38.30	31.85	30.40	0.94223	45.80	38.57	36.34	0.8554	83.00	77.00	65.89
0.95427	38.40	31.94	30.48	0.94206	45.90	38.66	36.42	0.8525	84.00	78.18	66.68
0.95413	38.50	32.03	30.56	0.94188	46.00	38.75	36.50	0.8496	85.00	79.40	67.47
0.95398	38.60	32.12	30.64	0.94170	46.10	38.84	36.58	0.8465	86.00	80.62	68.27
0.95383	38.70	32.20	30.72	0.94152	46.20	38.93	36.66	0.8435	87.00	81.85	69.06
0.95368	38.80	32.29	30.79	0.94134	46.30	39.03	36.74	0.8404	88.00	83.11	69.86
0.95353	38.90	32.37	30.87	0.94116	46.40	39.12	36.82	0.8372	89.00	84.38	70.65
0.95338	39.00	32.46	30.95	0.94098	46.50	39.21	36.90	0.8339	90.00	85.66	71.44
0.95323	39.10	32.55	31.03	0.94080	46.60	39.30	36.98	0.8306	91.00	86.97	72.23
0.95307	39.20	32.64	31.11	0.94062	46.70	39.39	37.06	0.8272	92.00	88.29	73.03
0.95292	39.30	32.72	31.18	0.94044	46.80	39.49	37.13	0.8236	93.00	89.61	73.82
0.95277	39.40	32.81	31.26	0.94026	46.90	39.58	37.21	0.8199	94.00	91.00	74.62
0.95262	39.50	32.90	31.34	0.94008	47.00	39.67	37.29	0.8161	95.00	92.41	75.41
0.95246	39.60	32.99	31.42	0.93990	47.10	39.76	37.37	0.8121	96.00	93.82	76.21
0.95231	39.70	33.08	31.50	0.93971	47.20	39.85	37.45	0.8079	97.00	95.29	77.01
0.95216	39.80	33.17	31.58	0.93953	47.30	39.95	37.53	0.8035	98.00	96.78	77.79
0.95200	39.90	33.27	31.66	0.93934	47.40	40.04	37.61	0.7989	99.00	98.37	78.59
0.95185	40.00	33.35	31.74	0.93916	47.50	40.13	37.69	0.7939	100.00	100.00	79.39
0.95169	40.10	33.44	31.82	0.93898	47.60	40.22	37.77				
0.95154	40.20	33.53	31.90	0.93879	47.70	40.32	37.85				
0.95138	40.30	33.61	31.98	0.93861	47.80	40.41	37.93				
0.95122	40.40	33.70	32.06	0.93842	47.90	40.51	38.01				

¹) Taken from LANGE, N. A., and FORKER, G. M., *Handbook of Chemistry*, Sandusky, 1949; and *Handbook of Chemistry and Physics*, Cleveland, 1954-55.

Man is a drop of dirty water (German proverb)

The vital functions of the highly developed organism are all closely dependent on the internal aqueous medium and on the maintenance therein of extreme constancy of chemical and physical properties. For the doctor a knowledge of the properties of aqueous solutions is therefore essential to an understanding of water and electrolyte balance and how it may be adjusted in pathological conditions.

The science of physical chemistry has now reached an advanced stage. It is unfortunate, however, that there are considerable gaps in our knowledge of this particular field. The properties of solutions with concentrations up to 0.01 mol/kg can now be calculated with great accuracy; for solutions with higher concentrations it is necessary to introduce empirical correction factors in order to reconcile measured with theoretical values. In biology and medicine, however, this is of little importance since the approximate formulae derived from theory are sufficiently accurate for most practical purposes.

The subject matter of this section should be regarded as complementary to the tables on pages 116–125 and to the section “Water and Electrolyte Balance” (pages 295–300).

Definition of the molecule

The concept of the molecule and the chemical units of measurement derived from it occupy an important position in the study of the properties of aqueous solutions.

By a molecule (from Latin *molecula*, a small mass) is meant the smallest part of a chemically homogeneous substance which possesses all the properties of that substance and which can exist in the free state in any phase (gas, solid, liquid, in solution). This definition is to be distinguished clearly from that of the atom, which is the smallest quantity of an element which is capable of entering into chemical combination.

The concept of the molecule thus embraces also the atoms of those elements which are capable of existing in the free state (for the conditions under which individual elements can exist in the free state see pages 82–97). The ions of dissolved salts, whether monatomic or polyatomic, can also be considered as molecules since in this phase they are very largely independent. One can accordingly speak quite correctly of monatomic and polyatomic molecules and of molecular and non-molecular atoms.

Units of measurement

The mole. The unit of measurement for molecules is the mole (international symbol: mol) and is defined as follows: 1 mole of an atomic or molecular substance is the mass of 6.023×10^{23} atoms or molecules¹. The mole is also often used as a purely quantitative unit, in which case it is the number 6.023×10^{23} molecules. The present tendency in physical chemistry is to follow the practice in physics and use the mole as a unit of mass, in which case the unit of quantity becomes the molar number n , e.g. 1 mol, 2 mol, 3 mol, etc., $n = 1, 2, 3$, etc.

The connection between the individual² chemical mass unit *mole* and the general physical mass unit *gram* is provided for polyatomic molecules by the molecular weight and for monatomic molecules by the atomic weight:

$$1 \text{ mol} = \frac{\text{molecular weight}}{(\text{atomic weight})} \times \text{gram} \quad (1)$$

The molecular weight is obtained from the empirical formula by adding together the atomic weights (for atomic weights see pages 82–97). The molecular weights of a number of medically important substances are given on pages 103 and 118.

The gram atom. For atomic substances and monatomic ions the expression gram atom (symbol: g. atom) is also in use. It is identical with the mole but may only be used for monatomic molecules. Since monatomic and polyatomic molecules usually occur together in physiological solutions it is preferable to use the expression mole for all the components.

The osmole. The osmole (symbol: osm) is a unit frequently used in biology and medicine but unknown in physical chemistry. It is not internationally recognized since it can be freely replaced by the mole. It represents the mass of 6.023×10^{23} osmotically active molecules in an aqueous solution and is therefore merely a mole related to the solution phase. It differs from the mole only when it refers to the undissociated substance. The degree of dissociation is dependent on many factors and is not a constant. In defining the osmole in relation to the undissociated substance it is therefore necessary to assume complete dissociation. The definition is given by

$$1 \text{ osmol}(\text{undiss. subst.}) = 1 \text{ mol}(\text{undiss. subst.})/\nu \quad (2)$$

where ν is the number of ions into which the undissociated substance breaks down on complete dissociation.

Since dissociation is never complete (either apparently or actually) the osmolar concentration of a substance never corresponds exactly to the right-hand side of equation (2). The osmole referring to the undissociated substance is therefore only suitable for rough calculations, while the osmolar concentration of a solution can be just as adequately expressed by the mole.

The gram equivalent. While the mole represents the mass of 6.023×10^{23} molecules, the gram equivalent (symbol: equ. or equiv)³ represents the mass of the quantity of ions with a total of 6.023×10^{23} valencies. The definition (cf. also page 75) is given by

$$1 \text{ gram equivalent} = 1 \text{ mole/valency} = \frac{\text{molecular weight}}{(\text{atomic weight})} \times \text{gram/valency} \quad (3)$$

Since the valency of polyvalent ions varies according to the reaction in which they are participating, the gram equivalent for such ions also varies according to the reaction. Should there be any doubt in such cases the reaction for which the gram equivalents have been calculated should be stated. In the case of substances which dissociate in stages it is necessary to base the gram equivalent calculations on an “average valency” (cf. for example phosphorus and serum proteins, page 120, right-hand column).

The gram equivalent is always indispensable in cases where acid-base relationships are being investigated.

Measures of concentration

Normality. By normality, (symbol: N) is meant the concentration in gram equivalents per litre of solution:

$$\text{Normality } N = n \frac{1000}{V} \quad (4)$$

where n = number of gram equivalents in the solution
 V = volume of the solution in millilitres

With polyvalent ions the normality too can vary according to the reaction (cf. gram equivalent). Titration data for 0.1-normal solutions of a number of substances are given on page 104.

Molarity, molality. By the molarity or molality of a solution is meant the concentration in moles per litre of solution or in moles per 1000 g water respectively:

$$\text{Molarity (per unit volume)} \epsilon = n \frac{1000}{V} \quad (5)$$

$$\text{Molality (per unit weight)} m = n \frac{1000}{n_0 M_0} \quad (6)$$

where n = molar number of the dissolved (undissociated) substance (in mixed solutions to be replaced by $\Sigma n = n_1 + n_2 + n_3 + \dots$, and m and ϵ to be designated Σm and $\Sigma \epsilon$), V = volume of the solution in ml, n_0 and M_0 = molar number and molecular weight of water ($n_0 M_0$ = weight of water).

In very dilute solutions molarity and molality are practically equal; at higher concentrations the difference between them is significant and is the greater, the greater the specific volume of the dissolved substance or substances. Thus the molarity of serum differs from the molality owing to the high specific volume of proteins. In order to calculate the molality of any particular serum component, the usual concentration figure, e.g. mg/100 ml serum, must be converted to give the concentration of this substance in the serum water.

This conversion can be made either by means of the specific gravity or by means of the protein content of serum. The former method is the more accurate and the appropriate factors are given on page 303. On the basis of protein content the conversion is made by means of the following formula⁴:

$$\text{Water content of serum in g/100 ml serum} = 98.40 \text{ minus } 0.718 \times \text{protein content (in g/100 ml serum)} \quad (7)$$

(The figure of 98.40 instead of 100 represents a correction for the volume occupied by inorganic and other constituents.)

For the calculation of osmotic relationships the molality is much more appropriate than the molarity since to a first approximation only the ratio of molecules of solute to molecules of water is important. If, for example, the molar concentration of the osmotically active particles of a moderately concentrated solution is determined by means of the freezing-point depression, the result obtained is for practical purposes identical with the molality.

Example: The freezing-point depression of serum is 0.56°C , corresponding to a molality of 300 mmol (300 mmol/1000 g water). The molarity of a normal serum is accordingly $300 \times 0.940 = 282 \text{ mmol/l}$ serum (table on page 303, factor in column 4 divided by 1000, spec. gravity 1.026).

Hereafter only the molality will be used. It should be noted that confusion between molality and molarity is sometimes found even in the best

¹) 6.023×10^{23} is AVOGADRO's number, known as LOSCHMIDT's number in the German-speaking countries. It varies slightly according to whether the mole is measured on the chemical or on the physical scale of atomic weights (cf. page 75 and the SMYTHE factor, page 80).

²) “Individual”, since the mass of a mole, which varies from substance to substance, is “individual”.

³) In the German-speaking countries the symbol “val” is used for gram equivalent.

⁴) PETERS, J. P., Water Balance in Health and Disease, in DUNCAN, *Diseases of Metabolism*, Philadelphia, 1953.

of the literature on this subject; it is therefore advisable to check on what is meant by the expression "molarity".

In order to avoid this confusion the molarity and molality should always be related to the *undissociated* substance; otherwise they should be clearly specified, e.g. "the molality of all osmotically active particles", etc.

Osmolarity, osmolality. These expressions signify the molar concentrations of all the osmotically active molecules in a solution. These two measures of concentration refer to the osmole and the remarks in the foregoing relating to this unit are applicable here also.

$$\text{Osmolarity (per unit volume)} = n \frac{1000}{V} \quad (8)$$

$$\text{Osmolality (per unit weight)} = n \frac{1000}{n_0 M_0} \quad (9)$$

where n = number of osmoles of the substance in the solution = number of moles of osmotically active particles of the substance in solution (in mixed solutions to be replaced by $\Sigma n = n_1 + n_2 + n_3 + \dots$), n_0 and M_0 = molar number and molecular weight of water.

In order to avoid confusion in the following text, the osmotically active concentration of a substance or mixture of substances which is to be expected on the basis of the structural formula and assumed complete dissociation will be designated the *ideal* osmolarity or osmolality. It is expressed by the product $n \times v$, where v = the number of individual particles into which a molecule of the undissociated substance breaks down on complete dissociation, and n = the molar (not osmolar) number of the undissociated substance. In mixtures $v n$ is to be replaced by $\Sigma v n = v_1 n_1 + v_2 n_2 + v_3 n_3 + \dots$.

Conversions. In order to avoid mistakes in decimal places, calculations should always be made using units having the same decimal:

mol \rightarrow equiv \rightarrow g \rightarrow °C \rightarrow atm, etc.
or mmol \rightarrow mg. equiv \rightarrow mg \rightarrow m°C \rightarrow matm, etc.

Calculations can also be made using only the dimensionless numbers n ; at the end of the calculation the result is converted into a dimensional magnitude by inserting the appropriate unit.

In the following text (to avoid confusion) the expressions n_{mol} , n_{equ} , n_{osm} , n_{g} are used to designate the numbers of moles, gram equivalents, etc. The osmole entering into the conversion calculations is the unit related to the undissociated substance. v = the number of particles into which a molecule breaks down on complete dissociation, z = valency of an ion, M = molecular weight.

Required	Given	Conversion	
n_{mol}	n_{g}	$n_{\text{mol}} = n_{\text{g}}/M$	(10)
	n_{osm}	$= n_{\text{osm}}/v$	(11)
	n_{equ}	$= n_{\text{equ}}/z$	(12)
n_{equ}	n_{g}	$n_{\text{equ}} = n_{\text{g}} \times z/M$	(13)
	n_{mol}	$= n_{\text{mol}} \times z$	(14)
	n_{osm}	$= n_{\text{equ}} \times z/v$	(15)
n_{osm}	n_{g}	$n_{\text{osm}} = n_{\text{g}}/v \times M$	(16)
	n_{mol}	$= n_{\text{mol}} \times v$	(17)
	n_{equ}	$= n_{\text{equ}} \times v/z$	(18)
n_{g}	n_{mol}	$n_{\text{g}} = n_{\text{mol}} \times M$	(19)
	n_{equ}	$= n_{\text{equ}} \times M/z$	(20)
	n_{osm}	$= n_{\text{osm}} \times v \times M$	(21)

These conversion formulae are also valid for concentrations, provided that a uniform definition of concentration is used throughout the calculation.

Electrolytes

By aqueous electrolytes are meant solutions of salts, acids and bases which by comparison with pure water have a high electrical conductivity (the expression electrolyte is also commonly used to denote the salts, acids and bases themselves, but strictly speaking it applies only to the solutions). All electrolyte-forming substances, designated electrolytes in the following text, dissociate in solution to a greater or lesser extent into electrically charged particles, known as ions. The positively charged ions, the cations, which migrate to the cathode in an electric field, are indicated by dots against the symbol (the number indicating the valency) and the negatively charged anions, which migrate to the anode, by dashes. Examples: magnesium ion = Mg^{++} , hydrogen ion = H^+ . These symbols are usual in physical chemistry but in the interests of a wider circle of readers have been replaced in these *Tables* by the more obvious signs + and -.

Two kinds of electrolytes are distinguished, strong and weak. The former are dissociated up to 50% in concentrated solution and practically completely in dilute solution; weak electrolytes never dissociate completely even in the

most dilute solutions. Among strong electrolytes are most neutral salts and strong acids such as hydrochloric, nitric and sulphuric acids. Most organic acids and bases (and carbonic acid) are weak electrolytes.

The dissociation of electrolytes is very markedly dependent on concentration; it increases with increasing dilution of the solution. Since the ions can be regarded as molecules the molecular concentration of an electrolyte is greater than its molar content of undissociated substance. On the assumption of complete dissociation the (ideal) concentration of all osmotically active particles is $v n$ (v = number of particles into which a molecule breaks down on complete dissociation, n = molar number of the undissociated substance). In reality the osmotic concentration is smaller by the factor g , so that:

$$\text{real} \begin{cases} \text{osmolarity} \\ \text{osmolality} \end{cases} = g \times \text{ideal} \begin{cases} \text{osmolarity} \\ \text{osmolality} \end{cases}$$

The factor g , known as the *osmotic coefficient*, can be calculated for very dilute solutions from the DEBYE-HÜCKEL theory but is mostly an empirically determined magnitude (see below). It is dependent not only on the concentration but also on the type of ions present, and increases with increasing valency of the ions.

These complicated relationships can with advantage be simplified for use with biological electrolytes:

a) the factor g is ignored and complete dissociation assumed. In the case of strong electrolytes this does not give rise to any considerable error; calculations are made using the ideal osmolarity or osmolality;

b) if the factor for the required concentration is known, it can be assumed that it is unaffected by the presence in a mixed solution of other kinds of ions; or

c) the osmotically active concentration is determined empirically.

Ideal and real solutions

The thermodynamic treatment of aqueous solutions is based on the concept of the ideal solution. For reasons of space it is impossible here to discuss the definition of this concept, suffice it to say that real solutions only approximate to ideal solutions at very low concentrations. To a first approximation the properties of an ideal solution (at constant temperature and pressure) change in proportion to the molecular concentration. It follows that the various properties also change in proportion to one another. In practice this circumstance is utilized in that the difficultly measurable osmotic pressure is calculated from the easily measurable freezing-point depression. The osmotically active concentration is therefore related not only to the osmotic pressure but also to the freezing-point depression, the boiling-point elevation, etc.

The osmotic pressure and freezing-point depression of ideal solutions are calculated as follows:

$$\text{Osmotic pressure (ideal)} = P_{\text{id}} = 0.08205 \times T \times v \times m \quad (22)^1$$

in atm

$$\text{Freezing-point depression (ideal)} = \Delta T_{\text{id}} = 1.858 \times v \times m \quad (23)^1$$

in °C

where 0.08205 = R = the gas constant in litre atmospheres, T = absolute temperature in °K = °C + 273.16, 1.858 = cryoscopic constant = molal freezing-point depression of water, v = number of particles into which a molecule breaks down on complete dissociation, m = the molality = moles of undissociated substance per 1000 g water¹. For conversion factors for pressure units see pages 60 and 61; for osmotic pressure and freezing-point depression for osmotic concentrations from 0-740 mmol/1000 g water, see page 116.

From (22) and (23) it follows that

$$P_{\text{(atm)}} = 0.0442 \times T \times \Delta T_{\text{(°C)}} \quad (24)$$

(T as in 22)

$$\text{or} \quad P_{\text{(atm, at °C)}} = 12.06 \times \Delta T_{\text{(°C)}} \quad (25)$$

In contrast to (22) and (23), equations (24) and (25) are valid for a wide range of concentrations and P and ΔT have therefore been written in place of P_{id} and ΔT_{id} .

Real solutions. As already mentioned the link between ideal and real solutions is formed by the osmotic coefficient g . This can now be determined by means of (23):

Osmotic coefficient

$$g = \frac{\Delta T}{\Delta T_{\text{id}}} = \frac{\Delta T}{1.858 v m} = \frac{\Delta T/n}{1.858 v} \quad (26)$$

where T = actual freezing-point depression;

n = molar number of the weighed or analytically determined substance (undissociated) in 1000 g water;

¹ In mixed solutions $v m$ is to be replaced by $\Sigma v m = \Sigma v n \frac{1000}{n_0 M_0}$ ($\Sigma v n = v_1 n_1 + v_2 n_2 + v_3 n_3 + \dots$).

Calculation of Freezing-point Depression and Osmotic Pressure

(continued from page 115)

T/n = so-called molecular freezing-point depression of the substance concerned ("molecular" related to the undissociated substance). Physico-chemical tables (*International Critical Tables, Handbook of Chemistry and Physics*, LANDOLT-BÖRNSTEIN) mostly give this molecular freezing-point depression, which requires only to be divided by $1.858 \times v$ to give g ;
 v = number of particles into which a molecule of the substance concerned breaks down on complete dissociation.

The osmotic coefficient g of one component of a mixed solution cannot, for example, be determined. In order to calculate the osmotic concentration of such a component it is assumed that g possesses the same magnitude as in a simple solution with the same osmolality as the solution in question.

The real osmolality is obtained from the real freezing-point depression according to equation (23) for the ideal freezing-point depression:
(real) osmolality = $\Delta T/1.858$ (27)

The ideal osmolality is obtained from the (real) osmolality by using the osmotic coefficient g :
ideal osmolality = real osmolality/ g (28)

This last equation is only required when it is desired to find the weight of a substance necessary to produce any given real osmolality. In other cases, when the weight is given, the ideal osmolality can always be calculated stoichiometrically ($v \times m$).

Applications

Calculation of the osmolality of blood serum from the freezing-point depression (0.56°C). According to (27) the real osmolality of serum = $0.56/1.858 = 301.4$ mmol (can be approximated to 300 mmol without sensible error).

For the calculation of freezing-point depression and osmotic pressure from the tonicity and vice versa, see the adjacent table.

Calculation of NaCl and glucose solutions (see table on page 117).
a) The weights of NaCl and glucose (or fructose) corresponding to given ideal osmolalities are obtained from columns 1/2 and 1/6. Column 7 gives the corresponding calorific values for glucose and fructose.

b) The ideal osmolalities corresponding to given weights of NaCl and glucose (or fructose) are obtained from columns 11/12 and 11/13. The corresponding calorific values for glucose and fructose are given in column 14.

c) The osmotic coefficients g (or $1/g$) are obtained for NaCl from columns 1/4 (or 1/5) and for glucose from columns 1/9 (or 1/10), the values in column 1 corresponding to real osmolalities.

Example 1. Required is the weight of NaCl necessary to yield a solution with a (real) osmolality of 500 mmol. From (28) the ideal osmolality = real osmolality/ $g = 500/0.9170 = 500 \times 1.0905 = 545.25$ mmol. The corresponding weight of NaCl from a) above lies between 15.783 and 16.075 at ca. 15.9 g. This is therefore the quantity of NaCl which must be dissolved in 1000 g water in order to yield an osmolality of 500 mmol.

The inconvenience of first calculating the ideal osmolality can be avoided by calculating the required weight direct from column 2 (for NaCl) or column 6 (for glucose). To do this the weight given in column 2 against the figure for the (real) osmolality looked for in column 1 is multiplied by the corresponding value for $1/g$. The above example, with a (real) osmolality of 500 mmol, thus gives the result: $14.613 \times 1.0905 = 15.935$ g NaCl.

Example 2. It is required to increase to 500 mmol the osmolality of a solution of 400 mmol by addition of NaCl. Here the calculation is simplified by assuming that the factor g does not change when the solution becomes a mixed solution. $1/g$ for NaCl for 500 mmol/1000 g water is 1.0905. Since 100 mmol are to be added by means of NaCl, the required weight (see paragraph 2 of example 1) is $2.923 \times 1.0905 = 3.188$ g NaCl.

d) **Exact calculation of isotonic solutions.** These can be calculated by the methods given in examples 1 and 2, or more simply from columns 1/3 (NaCl) and 1/8 (glucose).

Example 1. In order to obtain an isotonic NaCl or glucose solution (osmolality 300 mmol) 9.448 g NaCl or 53.399 g glucose must be dissolved in 1000 g water.

Example 2. It is required to render a solution of osmolality 200 mmol isotonic with serum by addition of NaCl, i.e. to increase the osmolality to 300 mmol. Since the additional osmolality is 100 mmol (column 1) the necessary weight of NaCl is 3.150 g (column 3).

The figure for glucose can be calculated in a similar manner.
The conversion tables on pages 118–120 are self-explanatory. The explanation of the tables on pages 124 and 125 is given on pages 121–123.

¹) Normal blood temperature = ca. 38°C = 311.16°K.

Real osmolality in mmol/1000 g water	Freezing-point depression T°C	Osmotic pressure		Freezing-point depression T°C	Real osmolality in mmol/1000 g water	Osmotic pressure	
		at 0°C atm	at 38°C ¹ atm			at 0°C atm	at 38°C ¹ atm
10	0.01858	0.22	0.26	0.01	5.38	0.12	0.14
20	0.03716	0.45	0.51	0.02	10.76	0.24	0.28
30	0.05574	0.67	0.78	0.03	16.15	0.36	0.41
40	0.07432	0.90	1.02	0.04	21.53	0.48	0.55
50	0.09290	1.12	1.28	0.05	26.91	0.60	0.69
60	0.11148	1.35	1.53	0.06	32.29	0.72	0.83
70	0.13006	1.57	1.79	0.07	37.68	0.84	0.96
80	0.14864	1.79	2.04	0.08	43.01	0.97	1.10
90	0.16722	2.02	2.30	0.09	48.44	1.09	1.24
100	0.18580	2.24	2.56	0.10	53.82	1.21	1.38
10	0.20438	2.47	2.81	0.11	59.20	1.33	1.51
20	0.22296	2.69	3.07	0.12	64.59	1.45	1.65
30	0.24154	2.91	3.32	0.13	69.97	1.57	1.79
40	0.26012	3.14	3.58	0.14	75.35	1.69	1.93
50	0.27870	3.36	3.83	0.15	80.73	1.81	2.06
60	0.29728	3.59	4.09	0.16	86.11	1.93	2.20
70	0.31586	3.81	4.34	0.17	91.50	2.05	2.34
80	0.33444	4.03	4.60	0.18	96.88	2.17	2.48
90	0.35302	4.26	4.86	0.19	102.26	2.29	2.61
200	0.37160	4.48	5.11	0.20	107.64	2.41	2.75
10	0.39018	4.71	5.37	0.21	113.02	2.53	2.89
20	0.40876	4.93	5.62	0.22	118.41	2.65	3.03
30	0.42734	5.16	5.88	0.23	123.79	2.77	3.16
40	0.44592	5.38	6.13	0.24	129.17	2.89	3.39
50	0.46450	5.60	6.39	0.25	134.55	3.02	3.44
60	0.48308	5.83	6.64	0.26	139.94	3.14	3.58
70	0.50166	6.05	6.90	0.27	145.32	3.26	3.71
80	0.52024	6.28	7.15	0.28	150.70	3.38	3.85
90	0.53882	6.50	7.41	0.29	156.08	3.50	3.99
300	0.55740	6.72	7.67	0.30	161.46	3.62	4.13
10	0.57598	6.95	7.92	0.31	166.85	3.74	4.26
20	0.59456	7.17	8.18	0.32	172.23	3.86	4.40
30	0.61314	7.40	8.43	0.33	177.61	3.98	4.54
40	0.63172	7.62	8.69	0.34	182.99	4.10	4.68
50	0.65030	7.84	8.94	0.35	188.38	4.22	4.81
60	0.66888	8.07	9.20	0.36	193.76	4.34	4.95
70	0.68746	8.29	9.45	0.37	199.14	4.46	5.09
80	0.70604	8.52	9.71	0.38	204.52	4.58	5.23
90	0.72462	8.74	9.97	0.39	209.90	4.70	5.36
400	0.74320	8.97	10.22	0.40	215.28	4.83	5.50
10	0.76178	9.19	10.47	0.41	220.67	4.95	5.64
20	0.78036	9.41	10.73	0.42	226.04	5.07	5.78
30	0.79894	9.64	10.99	0.43	231.43	5.19	5.91
40	0.81752	9.86	11.24	0.44	236.81	5.31	6.05
50	0.83610	10.09	11.50	0.45	242.20	5.43	6.19
60	0.85468	10.31	11.75	0.46	247.58	5.55	6.33
70	0.87326	10.53	12.01	0.47	252.96	5.67	6.46
80	0.89184	10.76	12.26	0.48	258.34	5.79	6.60
90	0.91042	10.98	12.52	0.49	263.72	5.91	6.74
500	0.92900	11.21	12.78	0.50	269.11	6.03	6.88
10	0.94758	11.43	13.03	0.51	274.49	6.15	7.01
20	0.96616	11.66	13.29	0.52	279.88	6.27	7.15
30	0.98474	11.88	13.54	0.53	285.25	6.39	7.29
40	1.00332	12.10	13.80	0.54	290.63	6.51	7.43
50	1.02190	12.33	14.05	0.55	296.02	6.63	7.57
60	1.04048	12.55	14.31	0.56	301.40	6.76	7.70
70	1.05906	12.78	14.57	0.57	306.78	6.88	7.84
80	1.07764	13.00	14.82	0.58	312.16	7.00	7.98
90	1.09622	13.22	15.08	0.59	317.55	7.12	8.11
600	1.11480	13.45	15.33	0.60	322.93	7.24	8.25
10	1.13338	13.67	15.59	0.61	328.31	7.36	8.39
20	1.15196	13.90	15.84	0.62	333.69	7.47	8.53
30	1.17054	14.12	16.10	0.63	339.07	7.60	8.66
40	1.18912	14.34	16.35	0.64	344.46	7.72	8.80
50	1.20770	14.57	16.61	0.65	349.84	7.84	8.94
60	1.22628	14.79	16.87	0.66	355.22	7.96	9.08
70	1.24486	15.02	17.12	0.67	360.60	8.08	9.21
80	1.26344	15.24	17.38	0.68	365.98	8.20	9.35
90	1.28202	15.47	17.63	0.69	371.37	8.32	9.49
700	1.30060	15.69	17.89	0.70	376.75	8.44	9.63
10	1.31918	15.91	18.14	0.71	382.13	8.56	9.76
20	1.33776	16.14	18.40	0.72	387.51	8.68	9.90
30	1.35634	16.36	18.65	0.73	392.90	8.81	10.04
40	1.37492	16.59	18.91	0.74	398.28	8.92	10.18

(see pages 114–116)

The values in columns 3, 4, 5, 8, 9 and 10 are calculated for the corresponding (real) osmotic concentrations (mmol or grams) per 1000 g water. See pages 114 and 115. The values of the osmotic coefficient *g* are interpolated from WASHBURN, E. W., (edit.) et al., *International Critical Tables*, Vol. IV, New York, 1928.

Osmolality (ideal)	Common salt, NaCl, mol. wt. 58.454				D-Glucose ¹ , C ₆ H ₁₂ O ₆ , mol. wt. 180.16						grams	Common salt NaCl	D-Glucose ¹ C ₆ H ₁₂ O ₆	
	corresponding to a weight of	at a freezing-point depression of 0.56°C (osmolality = 300 mmol) corresponds to a weight of	Osmotic coefficient for a real osmolality corresponding to the ideal value given in column 1	1/g	corresponding to a weight of	this weight corresponds to	at a freezing-point depression of 0.56°C (osmolality = 300 mmol) corresponds to a weight of	Osmotic coefficient for a real osmolality corresponding to the ideal value given in column 1	1/g	corresponds to an (ideal) osmolality of		corresponds to an (ideal) osmolality of	this weight corresponds to	
														mmol
mmol	grams	grams	g	1/g	grams	calories ²	grams	g	1/g	grams	mmol	mmol	calories ²	
10	0.292	0.315	0.9780	1.0225	1.802	7.53	1.780	1.0011	0.9989	1	34.22	5.55	4.18	
20	0.585	0.630	0.9699	0.310	3.603	15.07	3.560	0.011	9989	2	68.43	11.10	8.36	
30	0.877	0.945	0.9649	0.364	5.405	22.60	5.340	0.011	9989	3	102.65	16.65	12.55	
40	1.169	1.260	0.9607	0.409	7.206	30.14	7.120	0.011	9989	4	136.86	22.20	16.73	
50	1.461	1.574	0.9574	1.0445	9.008	37.67	8.900	1.0011	0.9989	5	171.08	27.75	20.91	
60	1.754	1.890	0.9546	0.476	10.810	45.21	10.680	0.011	9989	6	205.29	33.30	25.09	
70	2.046	2.205	0.9522	0.502	12.611	52.74	12.460	0.011	9989	7	239.51	38.85	29.27	
80	2.338	2.519	0.9500	0.526	14.413	60.27	14.240	0.011	9989	8	273.72	44.41	33.46	
90	2.630	2.834	0.9480	0.549	16.214	67.81	16.020	0.011	9989	9	307.93	49.96	37.64	
100	2.923	3.150	0.9462	1.0569	18.016	75.34	17.800	1.0011	0.9989	10	342.15	55.51	41.82	
10	3.215	3.464	0.9447	0.585	19.818	82.88	19.580	0.016	9984	11	376.36	61.06	46.00	
20	3.507	3.779	0.9434	0.600	21.619	90.41	21.360	0.021	9979	12	410.58	66.61	50.18	
30	3.800	4.095	0.9423	0.612	23.421	97.95	23.140	0.027	9973	13	444.79	72.16	54.37	
40	4.092	4.410	0.9413	0.624	25.222	105.48	24.920	0.032	9968	14	479.01	77.71	58.55	
50	4.384	4.724	0.9404	1.0634	27.024	113.01	26.700	1.0037	0.9963	15	513.22	83.26	62.73	
60	4.676	5.039	0.9395	0.644	28.826	120.55	28.480	0.042	9958	16	547.44	88.81	66.91	
70	4.969	5.355	0.9386	0.654	30.627	128.08	30.260	0.048	9952	17	581.65	94.36	71.09	
80	5.261	5.669	0.9377	0.664	32.429	135.62	32.040	0.054	9946	18	615.87	99.91	75.28	
90	5.553	5.984	0.9368	0.675	34.230	143.15	33.820	0.059	9941	19	650.08	105.46	79.46	
200	5.845	6.299	0.9360	1.0684	36.032	150.68	35.600	1.0065	0.9935	20	684.30	111.01	83.64	
10	6.138	6.614	0.9351	0.694	37.834	158.22	37.380	0.071	9930	21	718.51	116.56	87.82	
20	6.430	6.929	0.9342	0.704	39.635	165.75	39.120	0.077	9924	22	752.73	122.11	92.00	
30	6.722	7.244	0.9334	0.714	41.437	173.29	40.940	0.083	9918	23	786.94	127.66	96.19	
40	7.015	7.559	0.9326	0.723	43.238	180.82	42.720	0.089	9912	24	821.16	133.22	100.37	
50	7.307	7.874	0.9318	1.0732	45.040	188.36	44.500	1.0095	0.9906	25	855.37	138.77	104.55	
60	7.599	8.189	0.9310	0.741	46.842	195.89	46.280	0.101	9900	26	889.59	144.32	108.73	
70	7.891	8.503	0.9302	0.750	48.643	203.43	48.060	0.106	9895	27	923.80	149.87	112.91	
80	8.184	8.819	0.9295	0.759	50.445	210.96	49.840	0.112	9889	28	958.02	155.42	117.10	
90	8.476	9.124	0.9287	0.768	52.246	218.49	51.619	0.117	9884	29	992.45	160.97	121.28	
300	8.768	9.448	0.9280	1.0776	54.048	226.03	53.399	1.0122	0.9880	30	1026.45	166.52	125.46	
10	9.060		0.9273	0.784	55.850	233.56		0.126	9876	31	1060.66	172.06	129.64	
20	9.353		0.9266	0.792	57.651	241.10		0.132	9870	32	1094.88	177.62	133.82	
30	9.645		0.9259	0.800	59.453	248.63		0.138	9864	33	1129.09	183.17	138.01	
40	9.937		0.9252	0.808	61.254	256.17		0.143	9859	34	1163.31	188.72	142.19	
50	10.230		0.9245	1.0816	63.056	263.70		1.0148	0.9854	35	1197.52	194.27	146.37	
60	10.522		0.9238	0.824	64.858	271.23		0.153	9849	36	1231.74	199.82	150.55	
70	10.814		0.9232	0.832	66.659	278.77		0.158	9845	37	1265.95	205.37	154.73	
80	11.106		0.9226	0.839	68.461	286.30		0.163	9840	38	1300.17	210.92	158.92	
90	11.399		0.9220	0.846	70.262	293.84		0.167	9836	39	1334.38	216.47	163.10	
400	11.691		0.9214	1.0853	72.064	301.37		1.0172	0.9831	40	1368.60	222.03	167.28	
10	11.983		0.9209	0.859	73.866	308.91		0.176	9827	41	1402.81	227.58	171.46	
20	12.275		0.9204	0.865	75.667	316.44		0.180	9823	42	1437.03	233.13	175.64	
30	12.568		0.9199	0.871	77.469	323.98		0.184	9819	43	1471.24	238.68	179.82	
40	12.860		0.9194	0.877	79.270	331.51		0.187	9816	44	1505.46	244.23	184.00	
50	13.152		0.9190	1.0881	81.072	339.04		1.0191	0.9813	45	1539.67	249.78	188.19	
60	13.444		0.9186	0.886	82.874	346.58		0.194	9810	46	1573.89	255.33	192.37	
70	13.737		0.9182	0.891	84.675	354.11		0.197	9807	47	1608.10	260.88	196.55	
80	14.029		0.9178	0.896	86.477	361.64		0.200	9804	48	1642.32	266.43	200.74	
90	14.321		0.9174	0.900	88.278	369.18		0.203	9801	49	1676.53	271.98	204.92	
500	14.613		0.9170	1.0905	90.080	376.72		1.0207	0.9797	50	1710.74	277.53	209.10	
10	14.906		0.9167	0.909	91.882	384.25		0.210	9794	51	1744.96	283.08	213.28	
20	15.198		0.9164	0.912	93.683	391.78		0.213	9791	52	1779.18	288.63	217.46	
30	15.490		0.9161	0.916	95.485	399.32		0.216	9789	53	1813.39	294.18	221.65	
40	15.783		0.9158	0.919	97.286	406.85		0.219	9786	54	1847.61	299.73	225.82	
50	16.075		0.9155	1.0923	99.088	414.39		1.0222	0.9783	55	1881.82	305.28	230.01	
60	16.367		0.9152	0.927	100.890	421.92		0.225	9780	56	1916.03	310.84	234.19	
70	16.659		0.9149	0.930	102.691	429.45		0.228	9777	57	1950.25	316.39	238.37	
80	16.952		0.9146	0.934	104.493	436.98		0.231	9774	58	1984.47	321.94	242.56	
90	17.244		0.9143	0.937	106.294	444.52		0.233	9772	59	2018.68	327.49	246.73	
600	17.536		0.9140	1.0941	108.096	452.06		1.0236	0.9769	60	2052.90	333.04	250.92	
10	17.829		0.9137	0.945	109.898	459.59		0.238	9767	61	2087.11	338.59	255.10	
20	18.121		0.9134	0.948	111.699	467.13		0.241	9765	62	2121.33	344.14	259.28	
30	18.413		0.9131	0.952	113.501	474.66		0.243	9763	63	2			

a) **Given:** electrolyte. **Required:** molecular weight and maximum solubility in cold and hot water.
b) **Given:** weight of the undissociated substance. **Required:** millimoles of the undissociated substance, milligram equivalents (mg. equiv) and weight of the cation and anion, or milliosmoles of solute on the assumption of complete dissociation.

1 gram contains or corresponds to			Molecular weight	Undissociated substance mmol	Solubility ¹ g per 1000 g water		Cation			Anion			Milliosmoles ⁴
					cold	hot	mg. equiv	mg		mg. equiv	mg		
1	Calcium, Ca		40.08	24.95			49.90						
2	acetate	Ca(C ₂ H ₃ O ₂) ₂ + H ₂ O	176.18	5.68	436 ⁰	343 ¹⁰⁰	11.35	228	Ca ⁺⁺	11.35	670	C ₂ H ₃ O ₂ ⁻	17.03
3		Ca(C ₂ H ₃ O ₂) ₂ + 2H ₂ O	194.20	5.15	347 ²⁰	335 ⁸⁰	10.30	206	Ca ⁺⁺	10.30	608	C ₂ H ₃ O ₂ ⁻	15.45
4	chloride	CaCl ₂ + 2H ₂ O	147.03	6.80	977 ⁰	3260 ⁶⁰	13.60	273	Ca ⁺⁺	13.60	482	Cl ⁻	20.40
5	hydrated	CaCl ₂ + 6H ₂ O	219.09	4.56	2790 ⁰	5360 ²⁰	9.13	183	Ca ⁺⁺	9.13	324	Cl ⁻	13.69
6	citrate	Ca ₃ (C ₆ H ₅ O ₇) ₂ + 4H ₂ O	570.50	1.75	8.5 ¹⁸	9.6 ²³	10.52	211	Ca ⁺⁺	10.52	663	C ₆ H ₅ O ₇ ⁻⁻⁻	8.76
7	D-gluconate	Ca(C ₆ H ₁₁ O ₇) ₂ + H ₂ O	448.39	2.23	33 ¹⁵		4.46	89	Ca ⁺⁺	4.46	870	C ₆ H ₁₁ O ₇ ⁻	6.69
8	lactate	Ca(C ₃ H ₅ O ₃) ₂ + 5H ₂ O	308.30	3.24	31 ⁰	79 ³⁰	6.49	130	Ca ⁺⁺	6.49	578	C ₃ H ₅ O ₃ ⁻	9.73
9	laevulinate	Ca(C ₅ H ₇ O ₃) ₂ + 2H ₂ O	306.32	3.27	400		6.53	131	Ca ⁺⁺	6.53	752	C ₅ H ₇ O ₃ ⁻	9.79
10	oxide (lime) ²	CaO	56.08	17.83	1.31 ^{10d}	0.7 ^{80d}	35.66	715	Ca ⁺⁺				
11	phosphate, dibasic	CaHPO ₄ + 2H ₂ O	172.10	5.81	0.2 ²⁵	0.75 ¹⁰⁰	11.62	233	Ca ⁺⁺	11.62	558/180	HPO ₄ ⁻⁻ / P	11.62
12	thiosulphate	CaS ₂ O ₃ + 6H ₂ O	260.31	3.84	1000 ³	d	7.68	154	Ca ⁺⁺	7.68	431/246	S ₂ O ₃ ⁻⁻ / S	7.68
13	Chlorine, Cl		35.457	14.10			28.20						
14	Ammonium chloride	NH ₄ Cl	53.50	18.69	297 ⁰	758 ¹⁰⁰	18.69	337	NH ₄ ⁺	18.69	663	Cl ⁻	37.38
15	Hydrochloric acid (10% solution) 1 gram 1 millilitre See also Calcium (4, 5), Magnesium (17), Potassium (27) and Sodium (41).	(HCl) (0.1 g HCl) (0.1047 g HCl)	36.465 36.465	2.74 2.87	∞ ∞	∞ ∞	2.74 2.87	2.8 2.9	H ⁺ H ⁺	2.74 2.87	97.2 101.8	Cl ⁻ Cl ⁻	5.48 5.74
16	Magnesium, Mg		24.32	41.12			82.24						
17	chloride	MgCl ₂	95.23	10.50	542.5 ²⁰	727 ¹⁰⁰	21.00	255	Mg ⁺⁺	21.0	745	Cl ⁻	31.50
18		MgCl ₂ + 6H ₂ O	203.33	4.92	1670	3670	9.84	120	Mg ⁺⁺	9.84	349	Cl ⁻	14.75
19	hydroxide	Mg(OH) ₂	58.34	17.14	0.009 ¹⁸	0.04 ¹⁰⁰	34.28	417	Mg ⁺⁺				
20	oxide (magnesia) ²	MgO	40.32	24.80	0.0062	0.086 ³⁰	49.60	603	Mg ⁺⁺				
21	sulphate (Epsom salts)	MgSO ₄ + 7H ₂ O	246.50	4.06	710 ²⁰	910 ⁴⁰	8.11	98.7	Mg ⁺⁺	8.11	390/130	SO ₄ ⁻⁻ / S	8.11
22	Phosphorus, P See Calcium (11), Potassium (31, 32) and Sodium (36, 37, 46–48)		30.98	123.92			see p. 120						
23	Potassium, K		39.10	25.58			25.58						
24	acetate	K(C ₂ H ₃ O ₂)	98.14	10.19	2530 ²⁰	4920 ⁶²	10.19	398	K ⁺	10.19	602	C ₂ H ₃ O ₂ ⁻	20.38
25	bicarbonate	KHCO ₃	100.11	9.99	224	600 ⁶⁰	9.99	391	K ⁺	9.99	610	HCO ₃ ⁻	19.98
26	bromide	KBr	119.01	8.40	535 ⁰	1020 ¹⁰⁰	8.40	329	K ⁺	8.40	672	Br ⁻	16.81
27	chloride	KCl	74.55	13.41	347 ²⁰	567 ¹⁰⁰	13.41	525	K ⁺	13.41	476	Cl ⁻	26.83
28	citrate	K ₃ (C ₆ H ₅ O ₇) + H ₂ O	324.40	3.08	1670 ¹⁵	1997 ³¹	9.25	362	K ⁺	9.25	583	C ₆ H ₅ O ₇ ⁻⁻⁻	12.33
29	D-gluconate	K(C ₆ H ₁₁ O ₇)	234.25	4.27			4.27	167	K ⁺	4.27	833	C ₆ H ₁₁ O ₇ ⁻	8.54
30	oxide ²	K ₂ O	94.19	10.62	d	d	21.23	830					
31	phosphate, monobasic	KH ₂ PO ₄	136.09	7.35	330 ²⁵	v.s.	7.35 7.35	287 7.4	K ⁺ H ⁺	14.70	705/228	HPO ₄ ⁻⁻ / P	22.04
32	phosphate, dibasic	K ₂ HPO ₄	174.18	5.74	1670 ²⁰	v.s.	11.48	449	K ⁺	11.48	551/178	HPO ₄ ⁻⁻ / P	17.22
33	Sodium, Na		22.997	43.48			43.48						
34	acetate	Na(C ₂ H ₃ O ₂) + 3H ₂ O	136.09	7.35	762 ⁰	1388 ⁵⁰	7.35	169	Na ⁺	7.35	434	C ₂ H ₃ O ₂ ⁻	14.70
35	acid citrate	Na ₂ H(C ₆ H ₅ O ₇) + 1½H ₂ O	263.12	3.80	v.s.	v.s.	7.60 7.60 3.80 3.83	175 175 H ⁺	Na ⁺ Na ⁺ H ⁺	11.4	719	C ₆ H ₅ O ₇ ⁻⁻⁻	15.20
36	acid phosphate	NaH ₂ PO ₄ + H ₂ O	138.01	7.25	599 ⁰	427 ¹⁰⁰	7.25 7.25 7.25	167 167 7.3	Na ⁺ Na ⁺ H ⁺	14.49	696/224	HPO ₄ ⁻⁻ / P	21.74
37		NaH ₂ PO ₄ + 2H ₂ O	156.02	6.41	710 ⁰	3900 ⁸³	6.41 6.41 6.5	147 147 H ⁺	Na ⁺ Na ⁺ H ⁺	12.82	615/199	HPO ₄ ⁻⁻ / P	19.23
38	aminosalicylate	Na(C ₇ H ₆ O ₃ N) + 2H ₂ O	211.16	4.74			4.74	109	Na ⁺	4.74	720	C ₇ H ₆ O ₃ N ⁻	9.47
39	bicarbonate ³	NaHCO ₃	84.02	11.90	69 ⁰	164 ⁶⁰	11.90	274	Na ⁺	11.90	726	HCO ₃ ⁻	23.80
40	bromide	NaBr	102.91	9.72	795 ⁰	1210 ¹⁰⁰	9.72	224	Na ⁺	9.72	777	Br ⁻	19.43
41	chloride (common salt)	NaCl	58.45	17.11	357 ⁰	391 ¹⁰⁰	17.11	393	Na ⁺	17.11	607	Cl ⁻	34.22
42	citrate	Na ₃ (C ₆ H ₅ O ₇) + 2H ₂ O	294.12	3.40	720 ²⁵	1670 ¹⁰⁰	10.19	235	Na ⁺	10.19	643	C ₆ H ₅ O ₇ ⁻⁻⁻	13.60
43		Na ₃ (C ₆ H ₅ O ₇) + 5½H ₂ O	357.18	2.80	v.s.	v.s.	8.40	193	Na ⁺	8.40	529	C ₆ H ₅ O ₇ ⁻⁻⁻	11.20
44	lactate ³	Na(C ₃ H ₅ O ₃)	112.07	8.92	v.s.		8.92	205	Na ⁺	8.92	795	C ₃ H ₅ O ₃ ⁻	17.85
45	oxide ²	Na ₂ O	61.99	16.13	d	d	32.26	742	Na ⁺				
46	phosphate	Na ₂ HPO ₄	141.98	7.04			14.08	324	Na ⁺	14.08	676/218	HPO ₄ ⁻⁻ / P	21.13
47		Na ₂ HPO ₄ + 2H ₂ O	178.01	5.62	1000 ⁵⁰	1170 ⁸⁰	11.24	258	Na ⁺	11.24	539/174	HPO ₄ ⁻⁻ / P	16.85
48		Na ₂ HPO ₄ + 12H ₂ O	358.22	2.79	41.5	874 ³⁴	5.58	128	Na ⁺	5.58	268/86.5	HPO ₄ ⁻⁻ / P	8.38
49	salicylate	Na(C ₇ H ₅ O ₃)	160.11	6.25	1110 ¹⁵	1250 ²⁵	6.25	144	Na ⁺	6.25	856	C ₇ H ₅ O ₃ ⁻	12.49
50	sulphate (anhydrous)	Na ₂ SO ₄	142.06	7.04	47.6 ⁰	427 ¹⁰⁰	14.08	324	Na ⁺	14.08	676/226	SO ₄ ⁻⁻ / S	21.12
51	sulphate (Glauber's salt)	Na ₂ SO ₄ + 10H ₂ O	322.22	3.10	110 ⁰	927 ³⁰	6.21	143	Na ⁺	6.21	298/100	SO ₄ ⁻⁻ / S	9.31
52	thiosulphate	Na ₂ S ₂ O ₃	158.13	6.32	500	2310 ¹⁰⁰	12.65	291	Na ⁺	12.65	739/406	S ₂ O ₃ ⁻⁻ / S	18.97
53	Sulphur, S See Calcium (12), Magnesium (21) and Sodium (50–52)		32.066	256.53			see p. 120						

¹⁾ From *Handbook of Chemistry and Physics*, Cleveland, 1954–55. The index figures are the temperatures in °C; v.s. = very soluble; d = decomposes.
²⁾ The oxides have been included in view of the continuing use of the older nutritional tables.
³⁾ The sodium content of 1 gram sodium bicarbonate corresponds to that of 1.33 grams sodium lactate. The sodium content of 1 gram sodium lactate corresponds to that of 0.75 gram sodium bicarbonate.
⁴⁾ On the assumption of complete dissociation.

In collaboration with ESSELLIER, A. F., and JEANNERET, P., University Medical Clinic, Zurich (Prof. W. LÖFFLER).
(see pages 114–116)

Given: milliosmoles of the solute on the assumption of complete dissociation.

Required: weight and millimoles (mmol) of the undissociated substance, milligram equivalents (mg. equiv) and weight of the cation and anion.

10 Milliosmoles of the substance ¹ correspond to:			Undissociated substance		Cation			Anion		
			grams	mmol	mg. equiv	mg		mg. equiv	mg	
Calcium, Ca										
2	acetate	Ca(C ₂ H ₃ O ₂) ₂ + H ₂ O	0.587	3 ¹ / ₃	6 ² / ₃	134	Ca ⁺⁺	6 ² / ₃	394	C ₂ H ₃ O ₂ ⁻
3		Ca(C ₂ H ₃ O ₂) ₂ + 2H ₂ O	0.647	3 ¹ / ₃	6 ² / ₃	134	Ca ⁺⁺	6 ² / ₃	394	C ₂ H ₃ O ₂ ⁻
4	chloride	CaCl ₂ + 2H ₂ O	0.490	3 ¹ / ₃	6 ² / ₃	134	Ca ⁺⁺	6 ² / ₃	236	Cl ⁻
5	hydrated	CaCl ₂ + 6H ₂ O	0.730	3 ¹ / ₃	6 ² / ₃	134	Ca ⁺⁺	6 ² / ₃	236	Cl ⁻
6	citrate	Ca ₃ (C ₆ H ₅ O ₇) ₂ + 4H ₂ O	1.141	2	12	241	Ca ⁺⁺	12	756	C ₆ H ₅ O ₇ ⁻⁻⁻
7	D-gluconate	Ca(C ₆ H ₁₁ O ₇) ₂ + H ₂ O	1.495	3 ¹ / ₃	6 ² / ₃	134	Ca ⁺⁺	6 ² / ₃	1301	C ₆ H ₁₁ O ₇ ⁻
8	lactate	Ca(C ₃ H ₅ O ₃) ₂ + 5H ₂ O	1.028	3 ¹ / ₃	6 ² / ₃	134	Ca ⁺⁺	6 ² / ₃	594	C ₃ H ₅ O ₃ ⁻
9	laevulinate	Ca(C ₅ H ₇ O ₃) ₂ + 2H ₂ O	1.021	3 ¹ / ₃	6 ² / ₃	134	Ca ⁺⁺	6 ² / ₃	767	C ₅ H ₇ O ₃ ⁻
11	phosphate, dibasic	CaHPO ₄ + 2H ₂ O	0.861	5	10	200	Ca ⁺⁺	10	480	HPO ₄ ⁻⁻
									155	P
12	thiosulphate	CaS ₂ O ₃ + 6H ₂ O	1.302	5	10	200	Ca ⁺⁺	10	561	S ₂ O ₃ ⁻⁻
									321	S
Chlorine, Cl										
14	Ammonium chloride	NH ₄ Cl	0.268	5	5	90	NH ₄	5	177	Cl ⁻
15	Hydrochloric acid (10% solution)									
	1 gram	(0.1 g HCl/g)	1.823	5	5	5	H ⁺	5	177	Cl ⁻
	1 millilitre	(0.1047 g HCl/ml)	1.741	5	5	5	H ⁺	5	177	Cl ⁻
See also Calcium (4, 5), Magnesium (17), Potassium (27) and Sodium (41).										
Magnesium, Mg										
17	chloride	MgCl ₂	0.317	3 ¹ / ₃	6 ² / ₃	81	Mg ⁺⁺	6 ² / ₃	236	Cl ⁻
18		MgCl ₂ + 6H ₂ O	0.678	3 ¹ / ₃	6 ² / ₃	81	Mg ⁺⁺	6 ² / ₃	236	Cl ⁻
21	sulphate	MgSO ₄ + 7H ₂ O	1.233	5	10	122	Mg ⁺⁺	10	480	SO ₄ ⁻⁻
									160	S
Phosphorus, P										
22	See Calcium (11), Potassium (31, 32) and Sodium (36, 37, 46–48)									
Potassium, K										
24	acetate	K(C ₂ H ₃ O ₂)	0.491	5	5	196	K ⁺	5	295	C ₂ H ₃ O ₂ ⁻
25	bicarbonate	KHCO ₃	0.501	5	5	196	K ⁺	5	305	HCO ₃ ⁻
26	bromide	KBr	0.595	5	5	196	K ⁺	5	400	Br ⁻
27	chloride	KCl	0.373	5	5	196	K ⁺	5	177	Cl ⁻
28	citrate	K ₃ (C ₆ H ₅ O ₇) + H ₂ O	0.811	2 ¹ / ₂	7 ¹ / ₂	293	K ⁺	7 ¹ / ₂	473	C ₆ H ₅ O ₇ ⁻⁻⁻
29	D-gluconate	K(C ₆ H ₁₁ O ₇)	1.171	5	5	196	K ⁺	5	976	C ₆ H ₁₁ O ₇ ⁻
31	phosphate, monobasic	KH ₂ PO ₄	0.454	3 ¹ / ₃	3 ¹ / ₃	130	K ⁺	6 ² / ₃	320	HPO ₄ ⁻⁻
									103	P
32	phosphate, dibasic	K ₂ HPO ₄	0.581	3 ¹ / ₃	6 ² / ₃	261	K ⁺	6 ² / ₃	320	HPO ₄ ⁻⁻
									103	P
Sodium, Na										
34	acetate	Na(C ₂ H ₃ O ₂) + 3H ₂ O	0.681	5	5	115	Na ⁺	5	295	C ₂ H ₃ O ₂ ⁻
35	acid citrate	Na ₂ H(C ₆ H ₅ O ₇) + 1 ¹ / ₂ H ₂ O	0.658	2 ¹ / ₂	5	115	Na ⁺	7 ¹ / ₂	473	C ₆ H ₅ O ₇ ⁻⁻⁻
36	acid phosphate	NaH ₂ PO ₄ + H ₂ O	0.460	3 ¹ / ₃	3 ¹ / ₃	77	Na ⁺	6 ² / ₃	320	HPO ₄ ⁻⁻
37		NaH ₂ PO ₄ + 2H ₂ O	0.520	3 ¹ / ₃	3 ¹ / ₃	77	Na ⁺	6 ² / ₃	320	HPO ₄ ⁻⁻
									103	P
38	aminosalicylate	Na(C ₇ H ₆ O ₃ N) + 2H ₂ O	1.056	5	5	115	Na ⁺	5	761	C ₇ H ₆ O ₃ N ⁻
39	bicarbonate	NaHCO ₃	0.420	5	5	115	Na ⁺	5	305	HCO ₃ ⁻
40	bromide	NaBr	0.515	5	5	115	Na ⁺	5	400	Br ⁻
41	chloride	NaCl	0.292	5	5	115	Na ⁺	5	177	Cl ⁻
42	citrate	Na ₃ (C ₆ H ₅ O ₇) + 2H ₂ O	0.735	2 ¹ / ₂	7 ¹ / ₂	173	Na ⁺	7 ¹ / ₂	473	C ₆ H ₅ O ₇ ⁻⁻⁻
43		Na ₃ (C ₆ H ₅ O ₇) + 5 ¹ / ₂ H ₂ O	0.893	2 ¹ / ₂	7 ¹ / ₂	173	Na ⁺	7 ¹ / ₂	473	C ₆ H ₅ O ₇ ⁻⁻⁻
44	lactate	Na(C ₃ H ₅ O ₃)	0.560	5	5	115	Na ⁺	5	445	C ₃ H ₅ O ₃ ⁻
46	phosphate	Na ₂ HPO ₄	0.473	3 ¹ / ₃	6 ² / ₃	153	Na ⁺	6 ² / ₃	320	HPO ₄ ⁻⁻
									103	P
47		Na ₂ HPO ₄ + 2H ₂ O	0.593	3 ¹ / ₃	6 ² / ₃	153	Na ⁺	6 ² / ₃	320	HPO ₄ ⁻⁻
									103	P
48		Na ₂ HPO ₄ + 12H ₂ O	1.194	3 ¹ / ₃	6 ² / ₃	153	Na ⁺	6 ² / ₃	320	HPO ₄ ⁻⁻
									103	P
49	salicylate	Na(C ₇ H ₅ O ₃)	0.801	5	5	115	Na ⁺	5	686	C ₇ H ₅ O ₃ ⁻
50	sulphate (anhydrous)	Na ₂ SO ₄	0.474	3 ¹ / ₃	6 ² / ₃	153	Na ⁺	6 ² / ₃	320	SO ₄ ⁻⁻
									107	S
51	sulphate	Na ₂ SO ₄ + 10H ₂ O	1.074	3 ¹ / ₃	6 ² / ₃	153	Na ⁺	6 ² / ₃	320	SO ₄ ⁻⁻
									107	S
52	thiosulphate	Na ₂ S ₂ O ₃	0.527	3 ¹ / ₃	6 ² / ₃	153	Na ⁺	6 ² / ₃	374	S ₂ O ₃ ⁻⁻
									214	S
Sulphur, S										
53	See Calcium (12), Magnesium (21) and Sodium (50–52)									

¹) On the assumption of complete dissociation.

In collaboration with ESSELLIER, A. F., and JEANNERET, P., University Medical Clinic, Zurich (Prof. W. LÖFFLER).
(see pages 114–116)

a) Given: weight of the inorganic ions. Required: corresponding weight of the salt. – Left-hand column.
b) Given: milliequivalents of the ions. Required: corresponding weight of the salt. – Right-hand column.

Inorganic ions		
1	1 gram = 49.90 mg. equiv Calcium ⁺⁺ , Ca ⁺⁺ , corresponds to:	
2	4.396 g Calcium acetate	Ca(C ₂ H ₃ O ₂) ₂ + H ₂ O
3	4.845 g dihydrate	Ca(C ₂ H ₃ O ₂) ₂ + 2H ₂ O
4	3.668 g Calcium chloride	CaCl ₂ + 2H ₂ O
5	5.466 g hydrated	CaCl ₂ + 6H ₂ O
6	4.745 g Calcium citrate	Ca ₃ (C ₆ H ₅ O ₇) ₂ + 4H ₂ O
7	11.187 g Calcium D-gluconate	Ca(C ₆ H ₁₁ O ₇) ₂ + H ₂ O
8	7.692 g Calcium lactate	Ca(C ₃ H ₅ O ₃) ₂ + 5H ₂ O
9	7.643 g Calcium laevulinate	Ca(C ₅ H ₇ O ₃) ₂ + 2H ₂ O
11	4.294 g Calcium phosphate, dibasic	CaHPO ₄ + 2H ₂ O
12	6.495 g Calcium thiosulphate	CaS ₂ O ₃ + 6H ₂ O
1 gram Carbon dioxide, CO ₂ , corresponds to 1.387 g = 22.72 mg. equiv bicarbonate ions (HCO ₃ ⁻)		
*1 vol% Carbon dioxide, CO ₂ , at 0°C and 760 mm Hg corresponds to 27.40 mg/l = 0.449 mg. equiv/l bicarbonate ions (HCO ₃ ⁻)		
13	1 gram = 28.20 mg. equiv Chlorine ⁻ , Cl ⁻ , corresponds to:	
14	1.509 g Ammonium chloride	NH ₄ Cl
4	2.073 g Calcium chloride	CaCl ₂ + 2H ₂ O
5	3.090 g hydrated	CaCl ₂ + 6H ₂ O
15	10.28 g or 9.551 ml Hydrochloric acid, 10%	
17	1.343 g Magnesium chloride	MgCl ₂
18	2.867 g hexahydrate	MgCl ₂ + 6H ₂ O
27	2.103 g Potassium chloride	KCl
41	1.649 g Sodium chloride	NaCl
16	1 gram = 82.24 mg. equiv Magnesium ⁺⁺ , Mg ⁺⁺ , corresponds to:	
17	4.707 g Magnesium chloride	MgCl ₂
18	8.361 g hexahydrate	MgCl ₂ + 6H ₂ O
21	10.136 g Magnesium sulphate	MgSO ₄ + 7H ₂ O
22	1 gram Phosphorus, P, corresponds to:	
11	5.555 g Calcium phosphate, dibasic	CaHPO ₄ + 2H ₂ O
31	4.393 g Potassium phosphate, monobasic	KH ₂ PO ₄
32	5.622 g Potassium phosphate, dibasic	K ₂ HPO ₄
36	4.455 g Sodium acid phosphate	NaH ₂ PO ₄ + H ₂ O
37	5.036 g dihydrate	NaH ₂ PO ₄ + 2H ₂ O
46	4.583 g Sodium phosphate	Na ₂ HPO ₄
47	5.746 g dihydrate	Na ₂ HPO ₄ + 2H ₂ O
48	11.563 g dodecahydrate	Na ₂ HPO ₄ + 12H ₂ O
23	1 gram = 25.58 mg. equiv Potassium ⁺ , K ⁺ , corresponds to:	
24	2.510 g Potassium acetate	K(C ₂ H ₃ O ₂)
25	2.560 g Potassium bicarbonate	KHCO ₃
26	3.044 g Potassium bromide	KBr
27	1.907 g Potassium chloride	KCl
28	2.766 g Potassium citrate	K ₃ (C ₆ H ₅ O ₇) + H ₂ O
29	5.991 g Potassium D-gluconate	K(C ₆ H ₁₁ O ₇)
31	3.481 g Potassium phosphate, monobasic	KH ₂ PO ₄
32	2.227 g Potassium phosphate, dibasic	K ₂ HPO ₄
33	1 gram = 43.48 mg. equiv Sodium ⁺ , Na ⁺ , corresponds to:	
34	5.918 g Sodium acetate	Na(C ₂ H ₃ O ₂) + 3H ₂ O
35	5.721 g Sodium acid citrate	Na ₂ H(C ₆ H ₅ O ₇) + 1½H ₂ O
36	6.002 g Sodium acid phosphate	NaH ₂ PO ₄ + H ₂ O
37	6.784 g dihydrate	NaH ₂ PO ₄ + 2H ₂ O
38	9.182 g Sodium aminosalicilate	Na(C ₇ H ₆ O ₃ N) + 2H ₂ O
39	3.654 g Sodium bicarbonate	NaHCO ₃
41	2.542 g Sodium chloride	NaCl
42	4.263 g Sodium citrate	Na ₃ (C ₆ H ₅ O ₇) + 2H ₂ O
43	5.177 g Sodium citrate	Na ₃ (C ₆ H ₅ O ₇) + 5½H ₂ O
44	4.873 g Sodium lactate	Na(C ₃ H ₅ O ₃)
46	3.087 g Sodium phosphate	Na ₂ HPO ₄
47	3.870 g dihydrate	Na ₂ HPO ₄ + 2H ₂ O
48	7.788 g dodecahydrate	Na ₂ HPO ₄ + 12H ₂ O
49	6.962 g Sodium salicylate	Na(C ₇ H ₅ O ₃)
50	3.089 g Sodium sulphate (anhydrous)	Na ₂ SO ₄
51	7.006 g Sodium sulphate	Na ₂ SO ₄ + 10H ₂ O
52	3.438 g Sodium thiosulphate	Na ₂ S ₂ O ₃
53	1 gram Sulphur, S, corresponds to:	
12	4.059 g Calcium thiosulphate	CaS ₂ O ₃ + 6H ₂ O
21	7.687 g Magnesium sulphate	MgSO ₄ + 7H ₂ O
50	4.430 g Sodium sulphate (anhydrous)	Na ₂ SO ₄
51	10.049 g Sodium sulphate	Na ₂ SO ₄ + 10H ₂ O
52	2.466 g Sodium thiosulphate	Na ₂ S ₂ O ₃
1 mg. equiv = 20.04 mg Calcium ⁺⁺ , Ca ⁺⁺ , corresponds to:		
88.09 mg	Calcium acetate	Ca(C ₂ H ₃ O ₂) ₂ + H ₂ O
97.10 mg	dihydrate	Ca(C ₂ H ₃ O ₂) ₂ + 2H ₂ O
73.52 mg	Calcium chloride	CaCl ₂ + 2H ₂ O
109.55 mg	hydrated	CaCl ₂ + 6H ₂ O
95.08 mg	Calcium citrate	Ca ₃ (C ₆ H ₅ O ₇) ₂ + 4H ₂ O
224.20 mg	Calcium D-gluconate	Ca(C ₆ H ₁₁ O ₇) ₂ + H ₂ O
154.15 mg	Calcium lactate	Ca(C ₃ H ₅ O ₃) ₂ + 5H ₂ O
153.16 mg	Calcium laevulinate	Ca(C ₅ H ₇ O ₃) ₂ + 2H ₂ O
86.05 mg	Calcium phosphate, dibasic	CaHPO ₄ + 2H ₂ O
130.16 mg	Calcium thiosulphate	CaS ₂ O ₃ + 6H ₂ O
1 mg. equiv = 61.02 mg Bicarbonate ions (HCO ₃ ⁻) corresponds to 44.01 mg carbon dioxide (CO ₂)		
*1 mg. equiv/l = 61.02 mg/l Bicarbonate ions (HCO ₃ ⁻) corresponds at 0°C and 760 mm Hg to 2.23 vol% carbon dioxide (CO ₂)		
1 mg. equiv = 35.46 mg Chlorine ⁻ , Cl ⁻ , corresponds to:		
53.50 mg	Ammonium chloride	NH ₄ Cl
73.52 mg	Calcium chloride	CaCl ₂ + 2H ₂ O
109.55 mg	hydrated	CaCl ₂ + 6H ₂ O
364.7 mg or 348.28 µl	Hydrochloric acid, 10%	
47.62 mg	Magnesium chloride	MgCl ₂
101.67 mg	hexahydrate	MgCl ₂ + 6H ₂ O
74.55 mg	Potassium chloride	KCl
58.45 mg	Sodium chloride	NaCl
1 mg. equiv = 12.16 mg Magnesium ⁺⁺ , Mg ⁺⁺ , corresponds to:		
47.62 mg	Magnesium chloride	MgCl ₂
101.67 mg	hexahydrate	MgCl ₂ + 6H ₂ O
123.25 mg	Magnesium sulphate	MgSO ₄ + 7H ₂ O
** At pH 4.3 one gram Phosphorus, P, corresponds to 32.28 mg. equiv H ₂ PO ₄ ⁻ ions, and 1 mg. equiv of H ₂ PO ₄ ⁻ ions corresponds to 30.98 mg phosphorus.		
At pH 9.6 one gram Phosphorus, P, corresponds to 64.56 mg. equiv HPO ₄ ⁻⁻ ions, and 1 mg. equiv of HPO ₄ ⁻⁻ ions corresponds to 15.49 mg phosphorus.		
*** At pH 7.4 and 38°C 1 gram inorganic Phosphorus corresponds to 58.1 mg. equiv of phosphate ions, and 1 mg. equiv of Phosphate ions corresponds to 17.21 mg phosphorus (inorganic).		
1 mg. equiv = 39.10 mg Potassium ⁺ , K ⁺ , corresponds to:		
98.14 mg	Potassium acetate	K(C ₂ H ₃ O ₂)
100.11 mg	Potassium bicarbonate	KHCO ₃
119.01 mg	Potassium bromide	KBr
74.55 mg	Potassium chloride	KCl
108.13 mg	Potassium citrate	K ₃ (C ₆ H ₅ O ₇) + H ₂ O
234.25 mg	Potassium D-gluconate	K(C ₆ H ₁₁ O ₇)
136.09 mg	Potassium phosphate, monobasic	KH ₂ PO ₄
87.09 mg	Potassium phosphate, dibasic	K ₂ HPO ₄
1 mg. equiv = 22.997 mg Sodium ⁺ , Na ⁺ , corresponds to:		
136.09 mg	Sodium acetate	Na(C ₂ H ₃ O ₂) + 3H ₂ O
131.56 mg	Sodium acid citrate	Na ₂ H(C ₆ H ₅ O ₇) + 1½H ₂ O
138.01 mg	Sodium acid phosphate	NaH ₂ PO ₄ + H ₂ O
156.02 mg	dihydrate	NaH ₂ PO ₄ + 2H ₂ O
211.16 mg	Sodium aminosalicilate	Na(C ₇ H ₆ O ₃ N) + 2H ₂ O
84.02 mg	Sodium bicarbonate	NaHCO ₃
58.45 mg	Sodium chloride	NaCl
98.04 mg	Sodium citrate	Na ₃ (C ₆ H ₅ O ₇) + 2H ₂ O
119.06 mg	Sodium citrate	Na ₃ (C ₆ H ₅ O ₇) + 5½H ₂ O
112.07 mg	Sodium lactate	Na(C ₃ H ₅ O ₃)
70.99 mg	Sodium phosphate	Na ₂ HPO ₄
89.01 mg	dihydrate	Na ₂ HPO ₄ + 2H ₂ O
179.11 mg	dodecahydrate	Na ₂ HPO ₄ + 12H ₂ O
160.11 mg	Sodium salicylate	Na(C ₇ H ₅ O ₃)
71.03 mg	Sodium sulphate (anhydrous)	Na ₂ SO ₄
161.11 mg	Sodium sulphate	Na ₂ SO ₄ + 10H ₂ O
79.07 mg	Sodium thiosulphate	Na ₂ S ₂ O ₃
1 gram Sulphur, S, corresponds to 62.37 mg. equiv SO ₄ ⁻⁻ , and 1 mg. equiv SO ₄ ⁻⁻ corresponds to 16.03 mg sulphur.		
**** At pH 7.4 and 38°C and with an albumin/globulin ratio of 1.8, 1 gram of serum proteins corresponds to 0.241 basic mg. equiv of ionized serum proteins, and 1 basic mg. equiv of ionized serum proteins corresponds to 4.15 grams of serum proteins.		

* The conversion factors (0.449 and 2.23) given here for vol% CO₂ into mmol CO₂/l and mg. equiv CO₂/l (bicarbonate-CO₂) are derived from the molar volume of this gas (22.257 litres at 0°C and 760 mm Hg). The conversion factor 2.24 often used in medical literature is mistakenly based on the molar volume of ideal gases (22.412 l). For practical purposes the difference between these two factors is negligible. The same factor, rounded off to 2.226, is used on page 331.

** Basic equivalent of phosphates at pH values between 4.3 and 9.6, and therefore also at the physiological pH values in urine of 4.8–7.4.

*** After EDLBACHER-LEUTHARDT, *Lehrbuch der physiologischen Chemie*, Berlin, 1952.

**** After VAN SLYKE et al., *J. biol. Chem.*, **79**, 768, 1928.

By A. F. ESSELLIER and P. JEANNERET, University Medical Clinic, Zurich (Prof. W. LÖFFLER)¹
Bibliography: see page 124

On pages 124 and 125 will be found a summary of the commoner solutions for parenteral infusion, together with their sodium, potassium and chloride contents, as well as the lactate or bicarbonate, or ammonium-ion, contents. The (ideal) osmolarity* shows approximately how far the solution deviates from isotonia. A short discussion on the individual solutions and groups of solutions follows, with particular reference to the parenteral administration of potassium. No special attention has been paid to the replacement of magnesium, calcium and phosphate, the clinical significance of which with relation to parenteral replacement therapy with fluids and electrolytes requires further investigation. Commercial infusion fluids have not been included.

The object of this review is to provide, not a therapeutic schema, but a summary of information on the most important solutions mentioned in the literature. The data on ionic content and osmotic concentration have been set out in a uniform manner so as to simplify comparison and selection of solutions. The basis of a practical infusion therapy should be a number of well-chosen solutions which in various combinations (with supplementary ampoules for high-dosage calcium and potassium therapy) will suffice to meet all indications in parenteral water-, calorie- and electrolyte-replacement therapy³⁰. The clinically important solutions for parenteral calorie administration in the form of glucose-fructose, amino-acids and alcohol and for replacement of plasma colloids (dextran solutions, etc.), which are of great practical importance in the administration of electrolytes and water, have not been included in the table on pages 124 and 125.

When calorie administration by means of the infusion of carbohydrates is desired, any of the solutions listed for the intravenous administration of glucose, fructose or invert sugar can be used, with increase of total concentration up to 900–1200 mmol/l (each 100 g/l glucose or fructose = 555 mmol). See also page 117.

A. "Physiological solutions" (table on pages 124 and 125)

The object of the so-called physiological solutions is isotonia with serum or with a mixture resembling it. This condition is not indispensable in intravenous electrolyte therapy.

Isotonia. Strict isotonia is only necessary in medical research involving the perfusion of isolated organs. Clinically, it is desirable for subcutaneous infusions in order to avoid irritation of the tissues. As a result however of the rapid dilution of the infusion fluid which takes place in intravenous administration, considerable deviations from isotonia can be tolerated without irritation of the walls of the veins. For example, 20% invert-sugar solutions (ca. 1110 mosm/l), 2–2.5% salt solutions (513–769 mosm/l), mixtures such as 10% glucose solution with 3 g potassium chloride and 4 g salt (772 mosm/l), are well tolerated.

According to definition an infusion solution is isotonic with serum if it shows the same freezing-point depression ($\Delta T = 0.56^\circ\text{C}$; cf. discussion of this value by MICHAELS and MÜNZEL⁴⁰). On pages 114 and 115 will be found a definition of osmotic concentration together with the method of calculation. Isotonic osmotic concentrations for some electrolytes are given in footnote². It will

be seen from these figures that the usual infusion electrolytes are isotonic at an osmolarity* of ca. 310–330 mmol/l and glucose solution at ca. 290 mmol/l. The osmolarities* given in the last column of the table on pages 124 and 125 permit rapid calculation of the approximate osmotic relationships.

If electrolytes are combined with glucose solution for the purpose of increasing the calorie intake, the osmolarity* of the electrolytes must be added to that of the glucose. A 5.25% (isotonic) glucose solution corresponds to 291 mmol/l, a 10% glucose solution to 555 mmol/l.

Ionic composition. An isotonic infusion solution is actually only "physiological" if it has the same composition as blood serum. From the table on page 124 it will be seen that some of the solutions listed under A differ markedly in composition from blood serum (cf. "Water and Electrolyte Balance", pages 295–300). In infusion therapy with patients with sound kidneys this is without effect since the kidneys eliminate the surplus ions and thus prevent changes in the ionic composition of the extracellular fluid. On the contrary it is often advantageous to infuse solutions of composition different from that of serum in order to raise the intake of some mineral component. In the experimental perfusion of isolated organs on the other hand, the relationship between the cations Na^+ , K^+ and Ca^{++} is of importance.

– A 1. The so-called physiological salt solution contains Na- and Cl-ions in the proportion 1:1 while the proportion in serum water is 3:2 (cf. "Water and Electrolyte Balance"). Infusion of this solution in large quantities or with impaired kidney function thus has an acidifying effect³.

– A 2. The isotonic sodium lactate-salt solution (as modified by BUTLER⁶ and DARROW¹¹) is "physiological" both as regards isotonia and the ratio of the Na- and Cl-ions.

– A 3. a) The much-used glucose-salt solution can be employed to meet not only the requirement of sodium and chlorine but also to some extent that of water, which can only be partly met by isotonic salt solution.

The glucose or fructose of solutions of glucose, fructose and invert sugar is utilized in metabolism and the water of the solution is thereby available to meet the needs of the water balance.

– A 3. b) The solution a) can be improved by replacing 1 volume of isotonic salt solution by 1 volume of isotonic sodium lactate-salt solution (No. A 2).

If a greater calorie intake is desired, as is usually the case, the infusion solutions 3a and 3b can be made up with 10–20% glucose, fructose or invert-sugar solution instead of 5.25%. These solutions are then hypertonic and cannot therefore be used for subcutaneous administration. Glucose solution is being increasingly replaced by fructose solution because of the more efficient and rapid utilization of fructose compared to glucose (also in diabetes).

If administration of glucose is undesirable, salt solution should be diluted with distilled water instead of glucose solution. The resulting solution is hypotonic and naturally unsuitable for subcutaneous administration.

– A 4. In RINGER's solution the ratio of the Na- and Cl-ions is the same as in physiological salt solution; its potassium content is too small to meet the daily potassium requirement, so that it cannot be used in potassium replacement therapy. This and similar solutions (TYRODE's, RINGER-LOCKE, etc., see summaries of MICHAELS and MÜNZEL⁴⁰ and of HARTMANN²⁵, as well as solutions with supplementary magnesium and phosphate^{8,9,10,25}) are necessary in experimental physiology (perfusion of isolated organs) and also in cytological investigations. The clinical value of this group of solutions resembling blood serum in composition is uncertain; the role of calcium, magnesium and phosphate ions with relation to parenteral replacement therapy with water and electrolytes requires further investigation and the administration of these ions by means of infusion fluids is still largely based on theoretical considerations.

– A 5. In RINGER's lactate solution²⁵ the ratio of the Na- and Cl-ion concentrations is physiological. In extensive infusions it is therefore preferable to the usual RINGER's solution or to salt solution, particularly in cases of metabolic acidosis.

¹) In part by P. JEANNERET, H. ROSENMUND and A. F. ESSELLIER³⁰.

²)

	Osmotic concentration*			
	in 1000 g water		in 1 litre of solution	
	mmol	grams	mmol	grams
Sodium chloride**	325	9.5	325	9.5 (0.95%)
Ammonium chloride	327	8.75	325	8.7 (0.87%)
Sodium bicarbonate	314	13.2	312	13.1 (1.31%)
Glucose**	298	53.8	289	52.0 (5.20%)

In the table on pages 124 and 125 the values of MICHAELS and MÜNZEL⁴⁰ for sodium chloride (0.95%), sodium bicarbonate (1.40%) and glucose (5.25%) have been used. The values for the isotonic solutions of sodium lactate (1.75%) and ammonium chloride (0.83%) are based on measurements made in the chemical laboratory of the Medical Clinic (Director, Dr. H. ROSENMUND²⁰). The *Danish Pharmacopoeia IX* gives 1.72% for isotonic sodium lactate solution (see⁴⁸).

* Osmotic concentration (ideal), on the assumption of complete electrolytic dissociation. See pages 114 and 115.

** See also page 117.

Remarks on the table on pages 124 and 125 (continued)

– A 6. This solution contains Na- and Cl-ions in the “physiological” ratio of 14 : 10 and calcium ions in the same concentration as in serum. The content of potassium and magnesium is double that in serum. The potassium concentration is barely sufficient to meet the normal potassium demand by way of infusion (see below). For clinical purposes this solution nevertheless represents an advance over RINGER’s solution on account of its higher potassium content. Fox’s solution, however, contains no phosphate.

B. Solutions for the treatment of metabolic acidosis and alkalosis

The acidifying or alkalifying action of a salt depends on the metabolic utilization of its cation or anion, whereby the ion of opposite sign remains unabsorbed. The lactate ion is mainly converted in the liver into glycogen, the ammonium ion into urea.

– B 1. *Sodium lactate* solutions, which are stable and easily sterilized, are now very often used for the preparation of infusion solutions in place of sodium bicarbonate. *Sodium bicarbonate* solutions cannot be sterilized, so that the preparation of sterile solutions requires the use of dry sodium bicarbonate from ampoules. These are dissolved immediately before use by light agitation in the infusion fluid warmed to body temperature. 1 g sodium bicarbonate corresponds to 1.33 g sodium lactate, and 1 g sodium lactate corresponds to 0.75 g sodium bicarbonate. The bicarbonate or lactate solutions are usually administered diluted with glucose solution or distilled water. The combination with glucose solution is particularly indicated in renal acidosis. The alkalifying action of sodium lactate is adversely affected in cases of advanced lesions of the liver, when the breakdown of the lactate ion is retarded⁴³.

– B 2. The intravenous ammonium chloride treatment of alkalotic conditions has been described in detail by BODANSKY⁵. In cases of liver disease the intravenous administration of ammonium chloride can lead to temporary toxic reactions owing to the retarded breakdown of the ammonium ions⁴³. In practice this only occurs in cases of advanced lesions of the liver parenchyma since the conversion of ammonium salts into urea takes place even in the perfused isolated liver (LÖFFLER³⁶).

Since neither a sudden alkalification nor a sudden acidification is desirable, these solutions are in practice never used as such but only in combination with others.

The *practical calculation* of the quantity of an acidifying or alkalifying infusion solution to be administered^{5, 37} is based for adults on an average value for the water content of the body of 50% (cf. “Water and Electrolyte Balance”) and on a uniform intra- and extra-cellular distribution of bicarbonate ions⁴². Such calculations naturally yield only roughly approximate results, particularly since the question of the intracellular concentration of bicarbonate is not yet fully explained¹² (HASTINGS, quoted in ⁴⁴, page 24) and since chlorine ions are not distributed throughout all the body fluids²¹. These calculations can be simplified by reckoning in milliequivalents*.

With an average water content of 50%, 0.5 mg. equiv of alkali-fying or acidifying ions per kilogram body weight theoretically raises or lowers the alkali reserve by 1 mg. equiv/l = 2.23 vol%. Column 11 of the table gives for each solution the content of lactate/bicarbonate or ammonium ions, so that an indication of the amount of solution required to be infused in order to achieve the desired change in the alkali reserve can be obtained. For example, in order to increase or lower the alkali reserve in a patient weighing 70 kg by 6 mg. equiv a quantity of lactate/bicarbonate or ammonium ions of $70 \times 6 \times 0.5 = 210$ mg. equiv must be administered. In order to avoid the danger of an acidosis becoming converted into an alkalosis it is advisable not to attempt a complete normalization of the alkali reserve by means of an alkalifying solution¹². The latter should never be administered without supplementary potassium.

Since with children a higher water content of 66% must be reckoned with, the calculation in paediatrics yields infusion quantities which are relatively somewhat higher^{24, 26}. The differences between the calculated and observed effects of alkalifying^{24, 26} and

of acidifying compounds²¹ can be considerable since the above approximate calculation ignores a number of important factors.

In *diabetic acidosis* opinions differ as to the usefulness of intensive alkali therapy. BLAND⁴, BUTLER^{8, 9}, JOSLIN et al.³² advise caution; it is inadvisable to administer large quantities of sodium salts without potassium salts. On the other hand HARTMANN and ERGANIAN²⁷ have reported extremely good results in the intensive lactate treatment of diabetic coma. There is no doubt that a moderate alkali therapy is indicated in diabetic ketosis with very much lowered alkali reserve, since it has been shown that insulin activity is inhibited by acidosis^{22, 23, 20} and that acidosis increases the blood sugar³⁸.

C. Solutions for potassium replacement therapy

Potassium intake and elimination. On a normal diet the average daily potassium intake and elimination amounts to 77–102 mg. equiv (3–4 g), on a potassium-rich diet it can reach more than double this amount. On a completely potassium-free diet the potassium content of urine in healthy adults can fall to 1 mg. equiv/l (3.9 mg per cent) (FOURMAN¹⁸). In cases of severe illness, however, it is rare for the potassium content of the urine to fall below that of the serum⁴⁷; it has been shown that the tubular reabsorption of potassium can be affected by metabolic disturbances, particularly acidotic conditions and stress¹⁸. This defective regulation explains the frequent potassium deficiency observed during infusion therapy without potassium when sufficient of the element is available orally in food or medicines³². Potassium deficiency also arises through loss of fluids from the digestive tract (drainage, diarrhoea, vomiting). In the infusion treatment of diabetic coma considerable deficiencies may arise, amounting in adults to 300–400 mg. equiv (12–16 g). Other important causes of potassium deficiency are the administration of alkalifying sodium salts and high-dosage adrenocortical hormone therapy (see Corticotropin, page 187).

Prophylaxis of potassium deficiency. In purely parenteral alimention at least 30–40 mg. equiv (1.2–1.6 g) potassium per day should be administered *intravenously*, provided that potassium is eliminated only in the urine and that no other loss of potassium, e.g. by vomiting, diarrhoea, etc., is occurring and that no alkalifying sodium salts or adrenocortical hormones are being administered. When oral administration of potassium salts is impossible the potassium demand may be met simply by infusion of a solution of ca. 15–30 mg. equiv (0.6–1.2 g) potassium ions per litre. One litre of this solution should be administered over 4 hours (83 drops per minute). At this rate and concentration the administration of potassium is completely safe³⁵.

Treatment of potassium deficiency. With the treatment of an existing potassium deficiency it is necessary to distinguish between *acute* and *chronic* conditions. It has been shown that an acute potassium deficiency is of the order of 1.5–5 g (38–128 mg. equiv), a chronic deficiency of the order of 10–20 g (256–512 mg. equiv)³⁹, in exceptional cases up to 39 g (1000 mg. equiv)¹⁶. The correction of the deficit, however, requires greater amounts of potassium since the continuous elimination of the element must also be reckoned with. With a maximum daily potassium intake of 8–10 g with maintained diuresis, correction of the deficit always requires several days. In severe diabetic coma, according to MARTIN et al.³⁸, 6–8 g (153–205 mg. equiv) potassium should be administered during the first two days, initially intravenously, then as soon as possible orally. In cases of marked potassium deficiency with maintained diuresis TARAIL and ELKINTON⁴⁷ recommend infusion of up to 3.7 mg. equiv (145 mg) potassium per day per kilogram body weight, and DARROW and PRATT¹¹ up to 3 mg. equiv (117 mg) per day per kilogram.

Directions for infusion therapy. When diuresis is maintained and there is no adrenocortical insufficiency, any toxic effects arising are due not to the total amount administered but to the rate of intravenous administration.

According to TARAIL and ELKINTON^{16, 47} not more than 20 mg. equiv (782 mg) potassium per hour should be infused in adults; the same authors consider that 80 mg. equiv (3.12 g) potassium per litre of infusion solution is a safe concentration. KÜHLMAYER³⁴ has shown that up to 1 g (25.6 mg. equiv) potassium per hour can be administered intravenously without any significant increase of the serum potassium level. According to BODANSKY⁵

* See pages 114 and 115.

Remarks on the table on pages 124 and 125 (concluded)

a concentration of 40–90 mg.equiv (1.6–3.5 g) potassium per litre of infusion fluid is permissible with slow administration. DARROW and PRATT¹¹ regards 36 mg.equiv (1.4 g) potassium per litre of infusion fluid as a safe concentration. In paediatric therapy the same author dilutes his solutions to 12 mg.equiv/l. Potassium administration is not indicated in the initial infusions in the treatment of diabetic coma^{8,9,45}, during the first days after operation^{15,46}, in marked oliguria or anuria following traumatic shock, or after extensive muscular lesions⁴⁵.

For the routine treatment of potassium deficiency the administration of 30 mg.equiv (ca. 1.2 g) per litre of infusion solution over 4 hours (83 drops per minute*) is recommended. Comparison with the data given above shows that this dosage lies well outside the limits of toxicity. In severe cases this dosage may be doubled without hesitation.

Choice of potassium salt. There are no contraindications for potassium chloride, the commonest potassium salt, except in cases of renal hyperchloraemic acidosis. Alkalinifying potassium salts are the lactate⁸, the acetate^{19, 50, 41} and the gluconate¹.

Since intracellular loss of potassium is accompanied by loss of phosphates, use of a buffered potassium phosphate mixture with mono- and di-basic phosphate in the ratio of 1:4.5 has recently been recommended^{16, 17}. Infusion solutions should not contain more than 0.2 g phosphorus per litre⁹, however, so that mixtures of potassium phosphates with other potassium salts must be used.

On the basis of their observations, DAVIDSEN, KJERULF-JENSEN et al.^{13, 14} have made it a rule to limit the administration of potassium phosphate solutions to not more than 1 mg.equiv phosphate per 3 mg.equiv potassium. They have reported that too high a phosphate administration leads to the appearance of hyperphospheraemia and hypocalcaemia with tetanic attacks¹³.

Solutions with a high phosphate content are indicated for the treatment of marked potassium deficiencies only when the probability of intracellular loss of phosphates exists. This indication is based mainly on theoretical considerations and has not been confirmed clinically.

* In order to calculate the number of normal drops per minute necessary for the administration of x litres of infusion solution in 24 hours, multiply x by 13.9. This factor is approximately valid for all simple electrolytes and glucose solutions up to 20%.

C 1 and 5. With DARROW's potassium solutions it is possible to apply to adults the potassium therapy described above without too high a fluid loading resulting.

C 2a. BUTLER's earlier paediatric solution⁷ consisted of a hyper-tonic glucose solution (10%) with very low potassium, sodium and chloride content. This solution is contraindicated in diabetic coma so long as the glycaemia is not normalized. The solution contains so little potassium that it cannot meet the daily potassium demand in adults and is therefore useless for potassium replacement therapy; it contains 0.04 g phosphorus per litre as phosphate.

C 2b. BUTLER's new paediatric solution⁹ is also suitable for the treatment of adults. According to BUTLER the administration of this high-magnesium, -potassium and -phosphate solution is not indicated during the first hours of treatment of diabetic coma; instead the author recommends (for adults) the administration of about 1 litre of lactate-salt solution (solution A 2) diluted to half the concentration. This solution contains 5.2 mg.equiv magnesium and 0.21 g phosphorus per litre.

C 3 and 6. See the remarks above on phosphate administration. Both these solutions also figure in the *Danish Pharmacopoeia IX* (see ^{33, 48}).

C 4 and 7. These solutions contain too much phosphate (1.03 g phosphorus per litre); in solution C 4 potassium is present exclusively as potassium phosphate, so that high potassium dosage results in excessive phosphate intake¹³. In solution C 7, of 82.1 mg.equiv potassium 41.8 are present as phosphate, while not more than 1 mg.equiv in 3 of potassium should be administered as potassium phosphate¹³. The potassium content of solution C 7 lies at the upper limit of permissible concentration.

Ampoule solutions. Ampoule solutions of 30–40 mg.equiv potassium per litre can be used prophylactically and in the treatment of potassium deficiencies. One ampoule in one litre infused dropwise over 4 hours (83 drops per minute) is recommended as the normal dosage. (For choice of potassium salt, see above.)

D. Electrolyte replacement in loss of digestive tract secretions

Solutions D 1 and D 2 have approximately the same potassium-, sodium- and chloride-ion content as the average digestive tract secretions (cf. also "Water and Electrolyte Balance"). If a supplementary calorie intake is desired, the same amounts of electrolyte can be administered in 5–10% glucose solution.

Appendix: Sodium, potassium and chloride content of preserved blood and plasma

	Na +		K +		Cl-	
	mg. equiv	mg	mg. equiv	mg	mg. equiv	mg
Initial content of the plasma of freshly preserved blood:						
With anticoagulant solution 1 (sodium citrate [5½H₂O] 258.5 g, citric acid 76.1 g, glucose 333.3 g, distilled water to 10,000 ml):						
per 400 ml preserved whole blood ca.	43	990	0.850	30	17.5	620
per litre preserved plasma ca.	165	3800	3.300	130	67.5	2400
With anticoagulant solution 2 (sodium citrate [5½H₂O] 160 g, citric acid 47 g, glucose 250 g, distilled water to 10,000 ml):						
per 400 ml preserved whole blood ca.	36	830	0.850	30	17.5	620
per litre preserved plasma ca.	138	3180	3.30	130	67.5	2400
Content in a quantity of dried plasma yielding ca. 250 ml reconstituted citrate plasma:						
in the dried plasma ca.	34	780	0.9	40	18	640
in 1 litre of the reconstituted plasma ca.	137	3150	3.5	140	72	2560

Reconstituted dried plasma as well as the plasma of freshly preserved blood contains the electrolytes of the donor's plasma, to which must be added the electrolytes of the anticoagulant solution. Since the electrolyte level and haematocrit value of the donor's blood are unknown the electrolyte content of preserved blood and plasma can only be given approximately. The values in this table are based on the average normal values for sodium, potassium and chloride content of serum (cf. "Water and Electrolyte Balance"), on a haematocrit value of 45%, and on a mixture for the prepara-

tion of dried plasma consisting of ca. 310 ml of blood and ca. 90 ml of anticoagulant solution.

After 10 days' preservation under normal conditions, or even earlier, the potassium content of the plasma of preserved blood can rise to double the original level owing to the liberation of cell potassium. After 20 days the level can reach four times the original or more^{2, 49}.

The potassium content of the plasma is very variable even in

freshly preserved blood. Tests made in the chemical laboratory of the Clinic (Director, Dr. H. ROSENMUND³¹) have shown that in dissolved dried plasma, however, the potassium concentration largely agrees with the value calculated from the original mixture of blood and anticoagulant; the reason for this is that dried plasma is usually prepared immediately after separation from the donor's blood, before liberation of cell potassium takes place.

Bibliography: ¹) BERNHARD, A., *Science*, **113**, 751, 1951. ²) BEST, C. H., and TAYLOR, N. B., *Physiological Basis of Medical Practice*, Baltimore, 1950. ³) BLACK, D. A. K., *Lancet*, **1**, 353, 1953. ⁴) BLAND, J. H., *The Clinical Use of Fluid and Electrolyte*, Philadelphia and London, 1952. ⁵) BODANSKY, O., *Amer. J. med. Sci.*, **218**, 566, 1949. ⁶) BUTLER, A. M., and TALBOT, N. B., *N. Engl. J. Med.*, **231**, 586, 621, 1944. ⁷) BUTLER, A. M., et al., *Amer. J. Dis. Child.*, **72**, 481, 1946. ⁸) BUTLER, A. M., *Acta paediat.*, **38**, 59, 1949. ⁹) BUTLER, A. M., *N. Engl. J. Med.*, **243**, 648, 1950. ¹⁰) COOK, R. E., and CROWLEY, L. G., *N. Engl. J. Med.*, **246**, 637, 1952. ¹¹) DARROW, D. C., and PRATT, E. L., *J. Amer. med. Ass.*, **143**, 364, 432, 1950. ¹²) DARROW, D. C., and PRATT, E. L., *J. Pediat.*, **41**, 688, 1952. ¹³) DAVIDSEN, G., KJERULF-JENSEN, K., and KRARUP, N. B., *Lancet*, **1**, 375, 1951. ¹⁴) DAVIDSEN, G., and KJERULF-JENSEN, K., *Lancet*, **2**, 17, 1951. ¹⁵) ELIEL, L., PEARSON, O. H., and RAWSON, R. W., *N. Engl. J. Med.*, **243**, 471, 1950. ¹⁶) ELKINTON, J. R., and TARAIL, R., *Amer. J. Med.*, **9**, 200, 1950. ¹⁷) ELMAN, R. E., and WEICHELBAUM, T. E., *Ann. Surg.*, **135**, 164, 1952. ¹⁸) FOURMAN, P., *Lancet*, **1**, 1042, 1952. ¹⁹) FOX, C. L., et al., *J. Amer. med. Ass.*, **148**, 827, 1952. ²⁰) FRANÇOIS, R., and RUITON-UGLIENGO, *Presse méd.*, **62**, 867, 1954. ²¹) GOLDFINCH, N. K., and HOLZ, K. S., *Lancet*, **2**, 801, 1953. ²²) GUEST, G. M., *Amer. J. Med.*, **7**, 630, 1949. ²³) GUEST, G. M., MACKLER, B., and KNOWELES, H. C., *Diabetes*, **1**, 276, 1952. ²⁴) HARTMANN, A. F., and SENN, M. J. E., *J. clin. Invest.*, **11**, 327, 1932. ²⁵) HARTMANN, A. F., *J. Amer. med. Ass.*, **103**, 1349, 1934. ²⁶) HARTMANN, A. F., et al., *J. Pediat.*, **13**, 692, 1938. ²⁷) HARTMANN, A. F., and ERGANIAN, J., *J. Pediat.*, **31**, 274, 1947. ²⁸) HOEBER, R., *Physikalische Chemie der Zellen und Gewebe*, Berne, 1947. ²⁹) JEANNERET, P., ROSENMUND, H., and ESSELLIER, A. F., *Helv. med. Acta*, **21**, 191, 1954. ³⁰) JEANNERET, P., and ESSELLIER, A. F., *Die vorbeugende und korrektive parenterale Behandlung der Störungen des Wasser- und Elektrolythaushaltes mit Bemerkungen über die parenterale Kalorienzufuhr*. In preparation. ³¹) JEANNERET, P., ESSELLIER, A. F., and HOLTMEIER, H. J., *Die parenterale Kaliumbehandlung*. Indikationen und praktische Durchführung. In preparation. ³²) JOSLIN, E. P., ROOT, H. F., WHITE, P., and MARBLE, A., *The Treatment of Diabetes Mellitus*, Philadelphia, 1952. ³³) KOEFOED, H., *Svensk. farm. T.*, **61**, 266, 1951, reviewed by K. MÜNDEL in *Schweiz. Apoth. Ztg.*, **92**, 93, 1954. ³⁴) KÜHLMAYER, R., *Arch. klin. Chir.* (Langenbecks), **271**, 475, 1952. ³⁵) LANS, H. S., STEIN, I. F., and MEYER, K. A., *Surg. Gynec. Obstet.*, **95**, 321, 1952. ³⁶) LÖFFLER, W., *Biochem. Z.*, **85**, 230, 1918. ³⁷) MADDOCK, W. G., *Ohio med. J.*, **45**, 462, 1949. ³⁸) MARKEES, S., and MENEZER, A., *Schweiz. med. Wschr.*, **75**, 255, 1945. ³⁹) MARTIN, H. E., et al., *J. Amer. med. Ass.*, **147**, 24, 1951. ⁴⁰) MICHAELS, L., and MÜNDEL, K., *Pharm. Acta Helvet.*, **24**, 58, 199, 1949. ⁴¹) MUDGE, G. H., MANNING, J. A., and GILMAN, A., *Proc. Soc. exp. Biol.*, **71**, 136, 1949. ⁴²) PETERS, J. P., *Body Water. The Exchange of Fluids in Man*, Springfield, 1935. ⁴³) PETERS, J. P., and VAN SLYKE, D. D., *Quantitative Clinical Chemistry, I. Interpretations*, London, 1932. ⁴⁴) PETERS, J. P., and VAN SLYKE, D. D., *Quantitative Clinical Chemistry, I. Interpretations*, Baltimore, 1946. ⁴⁵) PLATTNER, H. C., *Le métabolisme du potassium et ses perturbations*, Paris, 1954. ⁴⁶) RANDALL, H. T., et al., *Surgery*, **26**, 341, 1949. ⁴⁷) TARAIL, R., and ELKINTON, J. R., *J. clin. Invest.*, **28**, 99, 1949. ⁴⁸) WALDOE, M., *Svensk. farm. T.*, **55**, 332, 1951, reviewed by LAUBER, R., and MÜNDEL, K., in *Schweiz. Apoth. Ztg.*, **91**, 833, 1953. ⁴⁹) WEISBERG, H. F., *Water, Electrolyte and Acid-Base Balance*, Baltimore, 1953. ⁵⁰) WINFIELD, J. M., FOX, C. L., and MERSHEIMER, W. L., *Ann. Surg.*, **134**, 625, 1951.

Summary of the commoner infusion solutions for water and electrolyte therapy†
See remarks on pages 121–123. For bibliography see above.

Solution	Na ⁺		K ⁺		Ca ⁺⁺		Mg ⁺⁺		Cl ⁻		Lactate-/bi-carbonate- or ammonium ⁺ ions	Phosphorus	Osmolarity (ideal) ***
	mg. equiv/l	mg/l	mg. equiv/l	mg/l	mg. equiv/l	mg/l	mg. equiv/l	mg/l	mg. equiv/l	mg/l			
	mg. equiv/l	mg/l	mg. equiv/l	mg/l	mg. equiv/l	mg/l	mg. equiv/l	mg/l	mg. equiv/l	mg/l	mg. equiv/l	mg/l	mmol/l
A. "Physiological" solutions													
1. Isotonic salt solution (0.95%)**	162.5	3733							162.5	5767	0		325
2. Isotonic sodium lactate*-salt solution: 1 vol. sodium lactate solution (1.75%) + 2 vols. salt solution (0.95%) (sodium lactate 5.83 g, sodium chloride 6.33 g, aqua dest. to 1000 ml)	160.3	3683							108.3	3842	— 52.0		321
3. a) Glucose-salt solution: 2 vols. isotonic glucose solution (5.25%) + 1 vol. isotonic salt solution (0.95%) (glucose 35.0 g, sodium chloride 3.16 g, aqua dest. to 1000 ml)	54.1	1242							54.1	1918	0		302
b)Glucose-sodium lactate-salt solution: 2 vols. isotonic glucose solution (5.25%) + 1 vol. isotonic sodium lactate-salt solution (glucose 35.0 g, sodium lactate 1.94 g, sodium chloride 2.11 g, aqua dest. to 1000 ml)	53.4	1227							36.1	1290	— 17.3		301
4. RINGER's solution after BEST and TAYLOR ² (sodium chloride 9.00 g, potassium chloride 0.30 g, hydrated calcium chloride 0.25 g, sodium bicarbonate 0.20 g, aqua dest. to 1000 ml)	156.4	3592	4.0	158	2.3	46			160.3	5687	— 2.4		324
5. RINGER's lactate solution after HARTMANN ²⁶ (sodium chloride 6.00 g, sodium lactate 3.05 g, potassium chloride 0.40 g, hydrated calcium chloride [6H ₂ O] 0.20 g, magnesium chloride [6H ₂ O] 0.20 g, aqua dest. to 1000 ml)	129.8	2983	5.4	210	1.8	37	2.0	24.0	111.8	3967	— 27.2		276
6. Solution of Fox et al. ^{19,50} ; prescription not given; organic anions as lactate and acetate, total 55 mg. equiv/l.....	140	3220	10	390	5	100.2	3	36.5	103	3660	— 55		316
B. Solutions for the correction of acidotic or alkalotic conditions													
Treatment of acidosis													
1. Isotonic sodium lactate solution* (1.75%) (sodium lactate 17.5 g, aqua dest. to 1000 ml)	156.1	3587									—156.1		312

*, **, *** See footnotes on the next page.
† Compiled by A. F. ESSELLIER and P. JEANNERET.

Solution	Na ⁺		K ⁺		Ca ⁺⁺		Mg ⁺⁺		Cl ⁻		Lactate ⁻ /bicarbonate ⁻ or ammonium ⁺ ions	Phosphorus	Osmolarity (ideal) ***
	mg. equiv/l	mg/l	mg. equiv/l	mg/l	mg. equiv/l	mg/l	mg. equiv/l	mg/l	mg. equiv/l	mg/l	mg. equiv/l	mg/l	mmol/l
<i>Treatment of alkalosis</i>													
2. Isotonic ammonium chloride solution (0.83%) (ammonium chloride 8.30 g, aqua dest. to 1000 ml)									155.1	5503	+ 155.1		310
2. Solutions for potassium replacement therapy													
<i>For administration in acidosis or in normal alkali reserve</i>													
1. DARROW's solution ^{5,11,16} (potassium chloride 2.70 g, sodium lactate* 5.80 g, sodium chloride 4.00 g, aqua dest. to 1000 ml)	120.2	2761	36.2	1417					104.7	3713	— 51.7		313
For infants DARROW recommends dilution of 1 vol. of this solution with 2 vols. isotonic glucose solution.....	40.7	920	12.1	472					34.9	1238	— 17.2		with 5.25% glucose: 299
2. a) BUTLER's paediatric solution ⁷ (potassium chloride 0.89 g, dibasic potassium phosphate 0.25 g, sodium lactate* 2.24 g, sodium chloride 0.58 g, 10% glucose solution to 1000 ml) ...	29.9	687	14.8	580					21.9	775	— 20.0	44.5	643
b) BUTLER's new paediatric solution ⁹ (potassium chloride 1.0 g, dibasic potassium phosphate 1.0 g, sodium lactate 2.8 g, sodium chloride 1.8 g, sodium acid phosphate [NaH ₂ PO ₄ ·1H ₂ O] 0.14 g, anhydrous magnesium chloride 0.25 g, 2–10% glucose solution to 1000 ml) (the magnesium chloride must be separately sterilized)	56.8	1304	24.9	974			5.3	63.8	49.5	1755	— 25.0	209.4	without glucose 167
3. Solution of DAVIDSEN and KJERULF-JENSEN ¹⁴ (potassium chloride 3.8 g, sodium acid phosphate [NaH ₂ PO ₄ ·2H ₂ O] 0.3 g, sodium phosphate [Na ₂ HPO ₄ ·2H ₂ O] 1.2 g, sodium lactate 10.3 g, aqua dest. to 1000 ml)	107.3	2465	51.0	1995					51.0	1809	— 91.9	269	312
4. Solution of ELKINTON and TARAIL ¹⁶ (dibasic potassium phosphate 4.5 g, monobasic potassium phosphate 1.0 g, sodium chloride 5.5 g, aqua dest. to 1000 ml)	94.1	2162	59.0	2307					94.1	3339	0	1029	288
<i>For administration in alkalosis or in normal alkali reserve</i>													
5. DARROW's solution ¹¹ (potassium chloride 2.70 g, sodium chloride 6.00 g, aqua dest. to 1000 ml)	102.6	2358	36.2	1418					138.8	4927	0		278
For infants DARROW recommends dilution of 1 vol. of this solution with 2 vols. isotonic glucose solution	34.2	786	12.0	473					46.3	1642	0		with 5.25% glucose: 287
6. Solution of DAVIDSEN and KJERULF-JENSEN ¹⁴ (potassium chloride 3.8 g, sodium acid phosphate [NaH ₂ PO ₄ ·2H ₂ O] 0.3 g, sodium phosphate [Na ₂ HPO ₄ ·2H ₂ O] 1.2 g, sodium chloride 5.4 g, aqua dest. to 1000 ml)	107.8	2476	51.0	1995					143.4	5087	0	269	313
7. Solution of ELKINTON and TARAIL ¹⁶ (potassium chloride 3.0 g, sodium chloride 4.2 g, dibasic potassium phosphate 3.2 g, monobasic potassium phosphate 0.7 g, aqua dest. to 1000 ml)	71.9	1651	82.1	3213					112.1	3977	0	729.2	295
D. Solutions for replacement of the digestive tract secretions													
1. Solution for replacement of gastric juice ¹⁰ (sodium chloride 3.70 g, potassium chloride 1.30 g, ammonium chloride 3.74 g, aqua dest. to 1000 ml)	63.3	1454	17.4	683					150.6	5344	+ 69.9		301
2. Solution for the replacement of alkaline secretions (bile and secretions of the pancreas and small intestine) ¹⁰ (sodium lactate* 5.60 g, sodium chloride 5.10 g, potassium chloride 0.90 g, aqua dest. to 1000 ml)	137.2	3152	12.1	473					99.4	3524	— 50.0		299

* If sodium lactate is not available or is contraindicated a freshly prepared sodium bicarbonate solution can be used instead: 1 dry ampoule of 14 g sodium bicarbonate freshly dissolved in 1 litre of sterile distilled water yields an isotonic sodium bicarbonate solution (14 g sodium bicarbonate = 167 mg. equiv Na, 333 mmol total concentration) (see remarks under B on page 122). For the preparation of lactate solutions see WALDOE¹⁸.

** All percentages given in the table relate to grams of the substance in 100 ml of solution.

*** Concentration of all osmotically active particles on the assumption of complete electrolytic dissociation. See pages 114 and 115.

For conversion factors for various substances in aqueous solution, see pages 114–120

1. Conversion factors for compounds

For converting	Factor	log ₁₀	For converting	Factor	log ₁₀
Acetone into acetoacetic acid ..	1.76	0.2455	Acetoacetic acid into acetone	0.57	0.7559-1
Acetone into 2-hydroxybutyric acid.....	1.79	0.2529	2-Hydroxybutyric acid into acetone	0.56	0.7482-1
Ca into CaO	1.4	0.1461	CaO into Ca	0.71	0.8513-1
Cl into NaCl	1.65	0.2175	NaCl into Cl	0.607	0.7832-1
K into K ₂ O	1.21	0.0828	K ₂ O into K	0.83	0.9191-1
Mg into MgO	1.66	0.2201	MgO into Mg	0.603	0.7803-1
Na..... into NaCl	2.54	0.4048	NaCl into Na.....	0.39	0.5911-1
Na..... into Na ₂ O	1.35	0.1303	Na ₂ O into Na.....	0.74	0.8692-1
P into P ₂ O ₅	2.29	0.3598	P ₂ O ₅ into P	0.44	0.6435-1
P into H ₃ PO ₄	3.16	0.4997	H ₃ PO ₄ into P	0.316	0.4997-1
S into SO ₃	2.55	0.4065	SO ₃ into S	0.40	0.6021-1
S into H ₂ SO ₄	3.06	0.4857	H ₂ SO ₄ into S	0.33	0.5185-1
Nitrogen					
Protein-N ... into protein	6.25	0.7959	Protein into protein-N...	0.16	0.2041-1
Ammonia-N . into ammonia	1.21	0.0828	Ammonia into ammonia-N .	0.82	0.9138-1
Creatine-N... into creatine	3.12	0.4942	Creatine into creatine-N ..	0.32	0.5051-1
Creatinine-N . into creatinine	2.7	0.4314	Creatinine..... into creatinine-N	0.37	0.5682-1
Urea-N..... into urea	2.14	0.3304	Urea into urea-N	0.47	0.6721-1
Uric acid-N .. into uric acid	3.0	0.4771	Uric acid..... into uric acid-N .	0.33	0.5185-1
Lipoids					
*Total lipid-P into phosphatides	23.5	1.3711			
Neutral fat-C . into neutral fats.....	1.32	0.1206	Neutral fats ... into neutral fat-C	0.757	0.8791-1
*Total lipid-C into total lipids	1.3	0.1139	Total lipids ... into *total lipid-C	0.769	0.8859-1
*Lipid-P into lecithin	2.6	0.4150	Lecithin / into *lipid-P	0.384	0.5843-1

2. Conversion of mg/100 ml into millimoles and inversely

$$\text{mmol/l} = \frac{10 \times \text{mg/100 ml}}{\text{molecular weight}} = \frac{10,000 \times \text{g/100 ml}}{\text{molecular weight}}$$
$$\text{mg/100 ml} = \frac{\text{mmol} \times \text{molecular weight}}{10}$$

3. Conversion of ccm of gas/100 ml into millimoles per litre

$$\text{mmol/l} = \frac{\text{ccm/100 ml}}{2.24} \quad (2.24 = \text{millimolar volume})$$
$$\text{ccm/100 ml} = 2.24 \times \text{mmol/l}$$

4. Conversion of mg/100 ml into milliequivalents per litre and inversely

$$\text{mg. equiv/l} = \frac{10 \times \text{mg/100 ml} \times \text{valency}}{\text{molecular weight}}$$
$$\text{mg/100 ml} = \frac{\text{mg. equiv/l} \times \text{molecular weight}}{10 \times \text{valency}}$$

5. N/1000 = 0.001-N = 1 ml N/10 per 100 ml = 1 ml N per litre = 1 mg. equiv per litre = 1 mmol per litre/valency = equivalent weight in mg per litre

* Lipids = phospholipids (phosphatides) + steroids.

If the measured volume of gas is denoted by $V_{p, t}$
where p = barometric pressure
 t = temperature

then the volume reduced to normal is given by the formula

$$V_n = K_{p \text{ (corrected), } t} \times V_{p, t}$$

Values of the factor K are given in table III below, against *corrected* barometric pressures.

Correction of barometric pressures

- From the observed barometer reading subtract:
- 1. Temperature correction (Table I) [for mercury barometers only, aneroid barometers are compensated].
 - 2. Correction for water vapour pressure (Table II).

I Temperature correction

II Water vapour correction

°C	Observed barometer reading in mm Hg												°C	Subtract from barometer reading at 100% humidity
	Brass scale									Glass scale				
	700	710	720	730	740	750	760	770	780	750	760	770		
15	1.71	1.74	1.76	1.78	1.81	1.83	1.86	1.88	1.91	1.95	1.97	2.00	15	12.8
16	1.82	1.85	1.88	1.90	1.93	1.96	1.98	2.01	2.03	2.08	2.10	2.13	16	13.6
17	1.94	1.97	1.99	2.02	2.05	2.08	2.10	2.13	2.16	2.21	2.23	2.26	17	14.5
18	2.05	2.08	2.11	2.14	2.17	2.20	2.23	2.26	2.29	2.33	2.37	2.40	18	15.5
19	2.17	2.20	2.23	2.26	2.29	2.32	2.35	2.38	2.41	2.46	2.50	2.53	19	16.5
20	2.28	2.31	2.34	2.38	2.41	2.44	2.47	2.51	2.54	2.59	2.63	2.66	20	17.5
21	2.39	2.43	2.46	2.50	2.53	2.56	2.60	2.63	2.67	2.72	2.76	2.79	21	18.6
22	2.51	2.54	2.58	2.61	2.65	2.69	2.72	2.76	2.79	2.85	2.89	2.93	22	19.8
23	2.62	2.66	2.69	2.73	2.77	2.81	2.84	2.88	2.92	2.98	3.02	3.06	23	21.1
24	2.73	2.77	2.81	2.85	2.89	2.93	2.97	3.01	3.05	3.11	3.15	3.19	24	22.4
25	2.85	2.89	2.93	2.97	3.01	3.05	3.09	3.13	3.17	3.24	3.28	3.32	25	23.7

III Correction factor K for normal volumes

Pressure (mm Hg)	Temperature											Logarithm of the correction factor	
	15° C	16° C	17° C	18° C	19° C	20° C	21° C	22° C	23° C	24° C	25° C		
700	0.87	0.87	0.87	0.86	0.86	0.86	0.85	0.85	0.85	0.85	0.84	84	9.9243-10
705	0.88	0.88	0.87	0.87	0.87	0.86	0.86	0.86	0.85	0.85	0.85	85	9.9294-10
710	0.88	0.88	0.88	0.88	0.87	0.87	0.87	0.86	0.86	0.86	0.85	86	9.9345-10
715	0.89	0.89	0.88	0.88	0.88	0.88	0.87	0.87	0.87	0.86	0.86	87	9.9395-10
720	0.90	0.89	0.89	0.89	0.88	0.88	0.88	0.88	0.87	0.87	0.87	88	9.9445-10
725	0.90	0.90	0.90	0.89	0.89	0.89	0.88	0.88	0.88	0.88	0.87	89	9.9494-10
730	0.91	0.91	0.90	0.90	0.90	0.89	0.89	0.89	0.88	0.88	0.88	90	9.9542-10
735	0.92	0.91	0.91	0.91	0.90	0.90	0.90	0.89	0.89	0.89	0.88	91	9.9590-10
740	0.92	0.92	0.92	0.91	0.91	0.91	0.90	0.90	0.90	0.89	0.89	92	9.9638-10
745	0.93	0.93	0.92	0.92	0.92	0.91	0.91	0.91	0.90	0.90	0.90	93	9.9685-10
750	0.93	0.93	0.93	0.92	0.92	0.92	0.92	0.91	0.91	0.91	0.90	94	9.9731-10
755	0.94	0.94	0.93	0.93	0.93	0.92	0.92	0.92	0.92	0.91	0.91	95	9.9777-10
760	0.95	0.94	0.94	0.94	0.93	0.93	0.93	0.92	0.92	0.92	0.92	96	9.9823-10
765	0.95	0.95	0.95	0.94	0.94	0.94	0.93	0.93	0.93	0.92	0.92	97	9.9868-10
770	0.96	0.95	0.95	0.95	0.94	0.94	0.94	0.93	0.93	0.93	0.92		
775	0.97	0.96	0.96	0.96	0.95	0.95	0.95	0.94	0.94	0.94	0.94		
780	0.97	0.97	0.97	0.96	0.96	0.96	0.95	0.95	0.95	0.94	0.94		
												Logarithms, see pages 8-11	

For bibliography, see the following page

Antibiotics now constitute the most powerful weapon for combating infectious diseases which the doctor possesses. They are in consequence being extensively applied, and in the USA, for example, their manufacture accounts for some two thirds in value of the entire production of pharmaceuticals. Generally speaking it is certain that in medical practice antibiotics are being too widely prescribed. Authoritative sources estimate that in 80% of the cases where they are applied either they are ineffective, or the severity of the infection does not justify their use, or another kind of drug of proved efficacy could have been used. This circumstance would be of no significance were it not for the tendency of pathogenic organisms to acquire resistance to antibiotics. Experience is showing that the increasing resistance exhibited by certain strains of bacteria constitutes a serious problem. Although this problem is not one which is likely at present to affect the individual doctor, it becomes strikingly manifest in large-scale investigations, in hospitals, and from a study of the literature on antibiotics. It cannot be too strongly emphasized that antibiotics should only be prescribed in cases where a definite effect on the organism concerned can be expected, or where the severity and course of the infection or the condition of the patient render their use imperative. It must also be borne in mind that treatment with antibiotics increases the general susceptibility of the body to illness for two reasons: firstly, rapid suppression of the infection also inhibits a possible acquisition of immunity (with increased danger of a relapse or reinfection); secondly (particularly where the tetracyclins*, with their broad antibacterial spectrum, are concerned) the natural balance of the bacterial flora may also be disturbed, resulting in a superinfection by normally apathogenic organisms which are resistant to the antibiotic and which have been able to multiply unhindered by their normal competitors. The principal agents causing superinfections are the staphylococci (see page 130) and thrush (*Candida albicans*, see page 168), particularly in young children and patients with lowered resistance. More and more cases are being reported of the successful treatment of the basic infection being followed by a resistant superinfection with extremely rapid and fatal course, or of the appearance of hitherto unknown pathological conditions such as staphylococcal dysentery.

Methods of administration

Systemic administration. When possible, antibiotics should be administered orally provided that they can be tolerated and that satisfactory resorption takes place, since side-effects are thereby reduced to a minimum. This applies not only to the tetracyclins*, erythromycin, carbomycin and chloramphenicol, but also, now that its price permits, to penicillin (5 times the parenteral dose), particularly for the treatment of children. Not only does oral penicillin produce considerably fewer allergic symptoms, its allergizing effect on the patient with respect to later treatment is much less, a factor of great importance where children are concerned. Streptomycin, polymyxin, neomycin and bacitracin are unsuited to systemic oral administration.

Intrathecal administration. Although much used earlier (owing to the high haematoencephalic barrier of some antibiotics) this method has shown itself for suitable antibiotics to be in no way superior to normal systemic administration (oral or parenteral). It should no longer be used, even in cases of tubercular meningitis.

Local application. On account of its allergizing tendency penicillin should here be replaced by antibiotics which are only rarely used systemically. Bacitracin plus neomycin, for example, are effective against the whole bacterial spectrum and well suited to local application. In this respect the sulphonamides and the many reliable disinfectants should not be overlooked. For washing and rinsing and as ointments they are often preferable, on account of their chemical stability, to antibiotics.

Dosage and toxicity

The dosage of the relatively non-toxic antibiotics (penicillin, erythromycin, carbomycin, tetracyclins) should in general be on the high side, so that any eventual bacterial resistance can either be encountered as early as possible or be prevented from developing. In the case of acute infections the antibiotic should be changed if

no marked effect on the infection has been observed after 24–48 hours. In view of their toxicity streptomycin, dihydrostreptomycin, chloramphenicol, polymyxin and neomycin should be administered with caution.

Dihydrostreptomycin damages the hearing function and streptomycin the equilibrium function of the ear. Since these effects are irreversible the danger limit of 0.5 gram (7.7 grains) per day (in prolonged treatment) should not be exceeded unless the condition of the patient justifies risking such lasting effects. Recently a 50:50 combination of streptomycin and dihydrostreptomycin has been suggested with the object of allowing higher doses without exceeding the danger limit for either component. It remains to be seen, however, whether this method would be justified in prolonged treatments, e.g. in tuberculosis. Used alone streptomycin is definitely preferable to dihydrostreptomycin, which should be avoided.

Chloramphenicol occasionally causes blood dyscrasia and its use should therefore be limited either to those cases where other antibiotics are ineffective or where it is specifically indicated, e.g. in typhoid and paratyphoid.

When administered parenterally polymyxin and neomycin are highly toxic, particularly to the kidneys, but not orally since they are not absorbed. Their use should be limited to special clinical indications such as *Proteus* or *Pseudomonas* infections and should be left in the hands of the internist.

Combinations of antibiotics are justified in those cases where experience shows clear evidence of synergy, or where the combination retards the acquisition by the organism of resistance to one of the components. The former applies for *Brucella* to the combination of streptomycin with one of the tetracyclins and for some other infections to the combination streptomycin plus penicillin. The latter applies for tuberculosis to the combinations streptomycin-PAS and streptomycin-isoniazid. However, since the substitution of a particular antibiotic by another equally effective one may avoid the development of resistance, the routine use of combinations, except when specifically indicated, is not to be recommended.

Details of the activity spectra of the antibiotics currently available and in general use are given in the tables on pages 129–168. Penicillin and the tetracyclins* suffice for the majority of pathogenic organisms. The three tetracyclins have about the same systemic toxicity, although oxytetracyclin is the most likely to produce toxic intestinal symptoms. The same applies to their activity. On the other hand differences in the effectiveness of these three antibiotics arise from their differing stability in aqueous solution: tetracyclin and oxytetracyclin are more stable than chlortetracyclin, with corresponding differences in their effectiveness (in intermittent treatment). Where resistance to penicillin occurs, erythromycin and carbomycin are suitable substitutes. Current antibiotics are ineffective against true viruses (cf. the aforementioned tables, pages 153–157). The favourable effects observed with some virus diseases are of an indirect nature for which there is as yet no accepted explanation, although it is presumably connected with a disturbance in the symbiotic relationship between bacteria and viruses. In spite of the lack of a direct effect, however, the application of antibiotics is recommended in those cases where there is a danger of secondary infections, e.g. in pneumonia and mumps. Favourable results have also been observed in the treatment of herpes zoster (shingles).

Although antibiotics are usually regarded as antibacterials, they are in some cases also effective against protozoa and worms. Thus strikingly successful results have been obtained with the tetracyclins in the treatment of intestinal amoebiasis (*Endamoeba histolytica*), of trichomoniasis and of oxyuriasis (*Enterobius vermicularis*). Here the effectiveness of the antibiotic apparently does not lie in direct destruction of the infecting organism. In the case of the amoeba the action is presumably due to destruction of certain bacteria essential to their growth; in the case of the oxyures the development of the egg is inhibited so that ovulation produces non-viable eggs.

Further information is given in the following tables. Although these have been based on an extensive bibliography no claim is made for their completeness. Particulars of the international units for certain antibiotics are given on page 79.

* Tetracyclins = tetracyclin, oxytetracyclin, and chlortetracyclin. These are new generic names which have been adopted following the establishment of the chemical structure of terramycin (oxytetracyclin) and aureomycin (chlortetracyclin).

For synonyms, see pages 172–178; for systematic classification, see pages 169–171.

On pages 129–168 will be found a summary in tabular form of pathogenic agents (bacteria, protozoa and worms), together with their synonyms, characteristics, susceptibility to antibiotics, anthelmintics, etc. This summary has been based on information derived from the following sources in addition to those referred to in the text: ALTEMEIER, A. A. (bone and joint infections), *J. Amer. med. Ass.*, **150**, 1463, 1952; ANDERSON et al. (erythromycin), *J. Amer. pharm. Ass.*, **41**, 555, 1952; BREED et al., *Bergey's Manual of Determinative Bacteriology*, 6th ed., Baltimore, 1948; BRUMPT, E., *Précis de Parasitologie*, 6th ed., Paris, 1949; CHANDLER, A. C., *Parasitology*, 7th ed., New York, 1946; ELEK et al., Laboratory Aspects of Combined Antibiotic Treatment, *Brit. med. J.*, **2**, 1298, 1953; ENGLISH et al. (carbomycin), *Antibiot. and Chemother.*, **2**, 678, 1952, *ibid.*, **3**, 307, 1953; FIEBIGER, J., *Tierische Parasiten*, 4th ed., Vienna, 1947; FINLAND, M., Clinical Uses of Currently Available Antibiotics, *Brit. med. J.*, **2**, 1115, 1953; FINLAND, M. (oxytetracyclin and chlortetracyclin) *Arch. intern. Med.*, **93**, 23, 1954; FINLAND, M. (tetracyclin), *J. Amer. med. Ass.*, **154**, 561, 1954; FINLAND and WILCOX (antibiotic combinations, etc.), *Proc. Soc. exp. Biol.*, **83**, 605, 1953; FLIPPIN and FOLTZ, The Newer Antimicrobial Agents, *Amer. Practit.*, **4**, 620, 1953; FLOREY, M. E., *The Clinical Application of Antibiotics (Penicillin)*, London, 1952; MCGUIRE et al. (erythromycin), *Schweiz. med. Wschr.*, **82**, 1064, 1952; HAIGHT, Th. H. (erythromycin and infections of the respiratory passages), *J. Lab. clin. Med.*, **43**, 15, 1954; HAVILLAND, J. W., Advances in Antibiotic Therapy, *Ann. intern. Med.*, **39**, 307, 1953; HERRELL, W. E. (antibiotics and circulatory and cardiac infections), *J. Amer. med. Ass.*, **150**, 1450, 1952; HUGHES, J. D. (antibiotics and infections of the intestinal tract), *J. Amer. med. Ass.*, **150**, 1456, 1952; KERN and WIMBERLEY, Penicillin Reactions, *Amer. J. med. Sci.*, **226**, 357, 1953; KIRBY, M. M. (erythromycin and staphylococci), *Arch. intern. Med.*, **92**, 464, 1953; KITCHEN and WAKSMAN, Streptomycin Therapy in Nontuberculous Diseases, *J. Amer. pharm. Ass.*, **62**, 522, 1953; MANSON-BAHR, Ph. H., *Tropical Diseases*, London, 1951; MILLER and WALKER, The Clinical Toxicity of Terramycin, *New Engl. J. Med.*, **249**, 479, 1953; *New and Nonofficial Remedies*, Council on Pharmacy and Chemistry (polymyxin), *J. Amer. med. Ass.*, **150**, 1219, 1952; ROMANSKY, G. A. (antibiotics and infections of the respiratory passages), *J. Amer. med. Ass.*, **150**, 1447, 1952; SCHNEIERSON, S. S. (resistance to aureomycin and chloramphenicol), *J. Lab. clin. Med.*, **40**, 48, 1952; SMITH et al. (erythromycin), *J. Amer. med. Ass.*, **151**, 805, 1953; STITT et al., *Practical Bacteriology, Hematology and Animal Parasitology*, 9th ed., Philadelphia, 1945; TRAFTON et al. (carbomycin), *New Engl. J. Med.*, **248**, 379, 1953; WAKSMAN, S. A. (streptomycin), *Science*, **118**, 259, 1953; WELCH et al., Bacterial Spectrum of Erythromycin, Carbomycin, Chloramphenicol, Aureomycin and Terramycin, *Antibiot. and Chemother.*, **2**, 249, 1952; WOMACK et al. (terramycin and infections of the urogenital tract), *Arch. intern. Med.*, **89**, 240, 1952; WRIGHT et al., Antibiotic Combinations, etc., *J. Lab. clin. Med.*, **42**, 877, 1953; YOW and MOYER, Toxicity of Polymyxin B, *Arch. intern. Med.*, **92**, 248, 1953.

- Legend:**
- Column 1: **Figures in bold type:** reference numbers corresponding to the **bold** figures in the “*Systematic Classification of Bacteria, Protozoa and Worms*” on pages 169–171. These numbers enable the appropriate genus, family, order, etc. to be found for any of the species listed in the tables.
- Column 2: *Figures in italics:* reference numbers corresponding to the *italic* figures in the “*Index of Pathogens and Infectious Diseases*” on pages 172–178. When information on any particular pathogen or infectious disease is desired, the appropriate *italic* figure is looked for in the tables.
- Column 3: Name and synonyms of the pathogen.
- Column 4: Characteristics of the pathogen.
- Column 5: Information on habitat, vectors, hosts, intermediate hosts, etc.
- Column 6: Disease or diseases caused by the pathogen.
- Column 7: Clinical application of antibiotics: 1 = to be administered primarily (drug of choice in **bold** type), 2 = to be administered as second choice, etc., 0 = no clinically significant effect, ? = effect unknown.
- Column 8: Remarks (other antibiotics, chemotherapeutics, anthelmintics and miscellaneous information).

See pages 169–171	See pages 172–178	Name Synonyms	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. appli- cation of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
10	1	Bacteria (Schizomycetes) <i>Pseudomonas aeruginosa</i> (SCHROETER) MIGULA <i>Bacille pyocyannique, Bacillus aeruginosus, Bacillus fluorescens, Bacillus pyocyaneus, Micrococcus pyocyaneus, Bacterium aeruginosum, Bacterium pyocyaneum</i>	–	facultative aerobe	Water, sewage, soil, also in air; intestinal tract, surface of skin	Suppurating wound infections (blue-green pus), frequent in chronic mixed infections, particularly with children: enteritis, infections of the urinary passages, also meningitis.		see remarks		Antibiotic of choice: polymyxin B ¹ . If unobtainable, best combination is terramycin + aureomycin; somewhat less effective, terramycin + chloramphenicol (t. + a. 12 times, t. + c. 9 times more effective than either alone). Penicillin + chloramphenicol are <i>antagonists</i> ² .
16	2	<i>Vibrio comma</i> (SCHROETER) WINSLOW et al. non-haemolytic: cholera vibrio haemolytic: El Tor vibrio <i>Bacillus cholerae, Bacillus comma, comma bacillus, Spirillum cholerae asiaticae, Vibrio cholerae asiaticae</i>	–	obligate aerobe	Intestinal contents of cholera patients, contaminated water	Cholera, El Tor.	0	2	1	The tetracyclins do not affect the cholera mortality rate significantly, although the vibrio is no longer present in the faeces after the third day of treatment. Antibiotic treatment is therefore mainly of epidemic-hygienic significance. Chloramphenicol less effective ³ .

¹) JAWETZ, E., *Arch. intern. Med.*, **89**, 80, 1952. ²) ARMSTRONG, C. W. J., *J. Lab. clin. Med.*, **37**, 584, 1951. ³) DAS et al., *Indian med. Gaz.*, **86**, 437, 1951.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. appli- cation of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
16	3	Bacteria (Schizomycetes) - continued Vibrio proteus BUCHNER <i>Microspira finkleri, Microspira protea, Pacinia finkleri, Spirillum finkleri, Vibrio finkleri</i>	-	facultative aerobe	Intestinal contents of patients, contaminated water	Cholera infantum, cholera nostras.	0	2	1	
21	4	Spirillum minus CARTER <i>Spirella muris, Spirella morsus muris, Spirillum minor, Spirochaeta japonica, Spirochaeta laverani, Spirochaeta morsus muris, Spirochaeta muris, Spirochaeta pettiti, Spirochaeta sodoku, Spironema laverani, Spironema minor, Spiroschaudinnia morsus muris, Treponema japonicum, Treponema laverani, Treponema minor, Treponema morsus muris, Treponema sodoku, Treponemella muris</i>	-	facultative aerobe	Rats and mice, widely disseminated	Classical rat-bite fever, sodoku, see also <i>Streptobacillus moniliformis</i> .	2	2	1	
27	5	Micrococcus pyogenes* var. aureus (ROSENBACH) ZOPF <i>Aurococcus aureus, Micrococcus aureus, Micrococcus lactis varians, Micrococcus pyogenes, Staphylococcus aureus, Staphylococcus pyogenes, Staphylococcus pyogenes aureus, staphylocoque</i>	+ In old cultures sometimes -	facultative aerobe	Surface of the skin, nasopharyngeal mucosa skin infections; also frequent in tonsillitis, sinusitis, otitis media, mastoiditis, osteomyelitis (over 80% of cases in acute haematogenic osteomyelitis, ca. 30% of cases in purulent arthritis ¹), mastitis; pyelitis, pyelonephritis, endocarditis; rarer in septicaemia (more frequent in the tropics) with secondary abscesses in liver, kidneys, and other organs. Often passes into the blood stream during the death struggle and is thus found in post-mortem blood cultures. During treatment with antibiotics (chlortetracyclin and oxytetracyclin) staphylococcic dysentery can appear (inhibition of normal flora, multiplication of resistant staphylococci). See remarks on page 129.	Commonest cause of abscesses, boils, whitlows, pemphigus neonatorum, and other	1	3	2	Staphylococci rapidly acquire penicillin resistance and large doses are therefore to be recommended; if ineffective, an immediate change to other antibiotics is indicated (see footnote*).
27	6	Micrococcus pyogenes var. albus (ROSENBACH) SCHROETER <i>Albococcus pyogenes, Micrococcus albus, Staphylococcus albus, Staphylococcus pyogenes albus</i>	+	facultative aerobe	Surface of the skin, nasopharyngeal mucosa	Saprophyte of the cutaneous surface, much less pathogenic than <i>M. aureus</i> . Causes similar infections, occasionally observed in fatal septicaemia.	1	3	2	

* Staphylococci and antibiotics

The resistance of staphylococci, not only with respect to penicillin but to all other known antibiotics, is increasing somewhat rapidly. For those antibiotics which have already been in intensive use for a considerable time, a high percentage of resistant strains is now observed, above all in hospitals: 60% for penicillin, the same proportion for the combination penicillin plus streptomycin, 40% for the tetracyclins^{2, 3}. Of hospital staffs 54% are nasal staphylococci carriers; 85% of the strains found on these persons have been shown to be penicillin-resistant³. These figures relate to conditions in American hospitals, in some cases since 1948, and can now be considered to be ubiquitous.

Against the more recently introduced antibiotics erythromycin and carbomycin only few strains are known to be resistant. Nevertheless it would be mistaken to treat every staphylococcal infection immediately with these antibiotics. In the first place 40% of all staphylococci still react to penicillin (still better to penicillin plus streptomycin⁴) and the proportion of penicillin-sensitive strains

seems to be stabilized at about this level. Secondly, the emergence of erythromycin- and carbomycin-resistant strains of staphylococci should be delayed for as long as possible. In this connection it is noteworthy that resistance to erythromycin increases very rapidly, that to carbomycin less rapidly. A cross-resistance between these two antibiotics is often observed⁵.

In the treatment of infections with the broad-spectrum tetracyclins a further factor is observed. As a result of the suppression or elimination by these antibiotics of the majority of gram-positive and gram-negative non-virulent or only slightly virulent bacteria, the balance of bacterial flora in the organism is seriously disturbed. Certain resistant bacterial strains are thereby given an opportunity to multiply unchecked, and so-called superinfections, often due to staphylococci, may arise. Patients in a very weakened condition are particularly susceptible to this danger, especially after operations, as are also old people and young children. The course of

(continued on next page)

¹) ALTEMEIER, W. A., *J. Amer. med. Ass.*, **150**, 1463, 1952. ²) NEEDHAM and NICHOLS, *J. Lab. clin. Med.*, **41**, 150, 1953. ³) DOWLING et al., *J. Amer. med. Ass.*, **157**, 327, 1955. ⁴) DOWLING et al., *J. Amer. med. Ass.*, **151**, 813, 1953. ⁵) WRIGHT et al., *J. Lab. clin. Med.*, **42**, 877, 1953.

For bibliography and legend, see page 129.

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. appli- cation of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) - continued								
27	7	Micrococcus citreus MIGULA <i>Micrococcus pyogenes citreus</i> , <i>Staphylococcus pyogenes citreus</i>	+	facultative aerobe	Surface of the skin, nasopharyngeal mucosa	Saprophyte of the cu- taneous surface, very low pathogenicity.	1	0	2	
27	8	Micrococcus aurantiacus (SCHROETER) COHN <i>Aurococcus aurantiacus</i> , <i>Bacteri- dium aurantiacum</i> , <i>Pediococcus aurantiacus</i> , <i>Sarcina aurantiaca</i> , <i>Staphylococcus aurantiacus</i> , <i>Streptococcus aurantiacus</i>	+	aerobe	Milk, cheese, dust	Isolated from skin in- fections.	1	0	2	
27	9	Micrococcus epidermidis (WINSLOW et WINSLOW) HUCKER <i>Albococcus epidermidis</i> , <i>Micro- coccus epidermidis albus</i> , <i>Staphy- lococcus epidermidis albus</i>	+	facultative aerobe	Skin and mucosa	Isolated from small abscesses due to skin punctures and other skin lesions.	1	0	2	
27	10	Micrococcus aerogenes (SCHOTTMÜLLER) BERGEY et al. <i>Staphylococcus aerogenes</i>	+	obligate anaerobe	Nose, pharynx, esp. tonsils, female genitals	Isolated in puerperal fever, tonsil infections.	1	0	2	
27	11	Micrococcus anaerobius comb. nov. (HAMM) <i>Staphylococcus anaerobius</i>	+	obligate anaerobe	Oral cavity, intestinal tract, urinary passages, vagina, con- junctiva	Isolated in cystitis, from inflamed tonsils.	1	0	2	
30	12	Gaffkya tetragena (GAFFKY) TREVISAN <i>Micrococcus tetragenus</i> , <i>Pedio- coccus tetragenus</i> , <i>Sarcina tetra- gena</i> , <i>Staphylococcus tetragenus</i> , <i>Tetracoccus septicus</i> , tétragène	+	facultative aerobe	Mucosa of the respiratory passages	Frequently found in sputum, together with other micro-organisms, particularly <i>Haemophilus influenzae</i> and tubercle bacilli. Pathogenicity doubtful.	1	?	?	
30	13	Gaffkya anaerobia (CHOUKÉVITCH) PRÉVOT <i>Micrococcus tetragenus anaero- bius</i> , <i>Tetracoccus anaerobius</i> , tétragène anaérobie	+	obligate anaerobe	All external body- cavities, esp. vagina	Isolated in puerperal in- fections, pathogenicity doubtful.	1	?	?	
31	14	Sarcina ventriculi GOODSIR <i>Merismopedia goodsirii</i> , <i>Meris- mopedia ventriculi</i> , <i>Sarcina beije- rincki</i> , <i>Zymosarcina ventriculi</i>	+	microaero- phil to anaerobe	Garden soil, dust, stomach	Non-pathogenic.	?	?	?	

such a staphylococcal superinfection is usually extremely rapid and the mortality high. In practice, however, the danger should not be overestimated. Generally speaking such infections are quite rare and, as already mentioned, mainly affect patients whose illness would in any case have taken a fatal course. The danger of possible superinfections provides no grounds for limiting the use of the broad-spectrum antibiotics.

The problem takes on a different aspect in gastrointestinal surgery. On the one hand the broad-spectrum antibiotics are almost indispensable for preoperative disinfection, on the other hand staphylococcal infections in the form of choleriform dysenteries are rather frequently observed (ca. 40% of staphylococci produce a strong enterotoxin¹). Clinical course: starting on the 1st to 4th day after operation, nausea, vomiting and moderate diarrhoea, developing rapidly into acute diarrhoea with profuse watery stool

(the diarrhoea may be absent) and followed by fever, lowered blood pressure, anuria and uraemia. Death occurs between the 3rd and 11th day after operation^{1,2} often with the clinical picture of shock. In preoperative disinfection it is therefore advisable to combine the tetracyclins with neomycin, which undergoes practically no resorption. This combination is extremely effective for the rapid elimination (avoidance of eventual development of resistance) of all anaerobic (by tetracyclins³) and aerobic (by neomycin⁴) organisms, including the tetracyclin-resistant staphylococci (neomycin⁵). Dosage⁶ (oral): first half-day (1½ days before operation) 4 times (1 g [15 grains] neomycin plus 0.25 g [4 grains] oxytetracyclin) at intervals of one hour, with mild laxatives. 2nd day (last day before operation) 4 times (1.5 g [23 grains] neomycin plus 0.25 g [4 grains] oxytetracyclin) spread over the day; colonic irrigation. 3rd day, operation.

¹) STILLWELL, G. C., *Minnesota Med.*, **36**, 63, 1953. ²) TERPLAN et al., *Gastroenterology*, **24**, 476, 1953. ³) DEARING and HEILMAN, *Proc. Mayo Clin.*, **25**, 87, 1950; DEARING and NEEDHAM, *ibid.*, **26**, 49, 1951. ⁴) DEARING and NEEDHAM, *Proc. Mayo Clin.*, **28**, 502, 1953. ⁵) DEARING and HEILMAN, *Proc. Mayo Clin.*, **28**, 121, 1953. ⁶) DEARING and NEEDHAM, *Proc. Mayo Clin.*, **28**, 503, 1953.

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. application of antibiotics			Remarks
			GRAM'S staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) – continued								
32	15	Neisseria gonorrhoeae TREVISAN <i>Diplococcus gonorrhoeae</i> , gonococcus, <i>Merismopedia gonorrhoeae</i> , <i>Micrococcus gonococcus</i> , <i>Micrococcus gonorrhoeae</i>	–	aerobe to facultative anaerobe		Gonorrhoea, ophthalmoblenorrhoea of newborn.	1	2	2	1 × 1 million I.U. procaine-penicillin i.m. or 2 × 1 g (15 grains) oxy-tetracyclin orally suffice to cure gonorrhoea. Instillation of penicillin solution in the eyes is as effective (and prophylactic) against newborn ophthalmoblenorrhoea as instillation of silver nitrate solution.
32	16	Neisseria meningitidis (ALBRECHT et GHON) HOLLAND <i>Diplococcus intracellularis</i> , <i>Diplococcus intracellularis meningitidis</i> WEICHELBAUM, <i>Diplococcus meningitidis</i> , meningococcus, <i>Meningococcus intracellularis</i> , <i>Micrococcus intracellularis</i> , <i>Micrococcus meningococcus cerebrospinalis</i> , <i>Neisseria intracellularis</i> , <i>Neisseria weichselbaumii</i>	–	aerobe	Human nasopharynx	Epidemic cerebrospinal meningitis (70% of all cases of acute meningitis), also sepsis without meningital symptoms: high fever, purpura, adrenal haemorrhages with severe shock (WATERHOUSE-FRIEDRICHSEN syndrome).	1	0	2	Sulphonamides are rather more effective than penicillin and should therefore be combined with this or any other antibiotic used.
32	17	Neisseria catarrhalis (FROSCH et KOLLE) HOLLAND <i>Diplococcus pharyngis communis</i> , <i>Micrococcus catarrhalis</i>	–	facultative aerobe	Mucosa of the respiratory passages	Often found, with other organisms, in mucous inflammations of the respiratory passages.	1	0	2	
32	18	Neisseria sicca (VON LINGELSHEIM) BERGEY et al. <i>Diplococcus pharyngis siccus</i> , <i>Micrococcus pharyngis siccus</i> , <i>Neisseria pharyngis-sicci</i>	–	facultative aerobe	Mucosa of the respiratory passages	Saprophyte.	1	0	2	
32	19	Neisseria perflava BERGEY et al.	–	facultative aerobe	Mucosa of the respiratory passages	Saprophyte.	1	0	2	
32	20	Neisseria flava BERGEY et al.	–		Mucosa of the respiratory passages	Saprophyte. Also found (very rarely) in cerebrospinal fluid in meningitis.	1	0	2	
32	21	Neisseria subflava BERGEY et al.	–	facultative aerobe	Mucosa of the respiratory passages	Easily mistaken for <i>Neisseria meningitidis</i> (16) Non-pathogenic.	1	0	2	
32	22	Neisseria flavescens BRANHAM	–	facultative aerobe	Probably mucosa of the respiratory passages	Found in cerebrospinal fluid in meningitis.	1	0	2	
32	23	Neisseria discoides PRÉVOT	–	obligate anaerobe	Mouth cavity, respiratory passages	Non-pathogenic.	1	0	2	
32	24	Neisseria reniformis (COTTET) PRÉVOT <i>Diplococcus reniformis</i> , <i>Micrococcus reniformis</i>	–	obligate anaerobe	?	Pathogenic. Isolated in several cases of inflammation of the urogenital system.	1	0	2	
33	25	Veillonella parvula (VEILLON et ZUBER) PRÉVOT <i>Micrococcus parvulus</i> , <i>Staphylococcus parvulus</i>	–	obligate anaerobe	Saprophytic in body-cavities, esp. mouth and intestinal tract	Can become pathogenic. Isolated in pulmonary gangrene, abscesses, alveolar suppuration.	1	?	2	
33	26	Veillonella gazogenes (HALL et HOWITT) MURRAY <i>Micrococcus alcalescens</i> , <i>Micrococcus gazogenes alcalescens</i> anaerobius, <i>Veillonella alcalescens</i>	–	obligate anaerobe	Usually in saliva	Not normally pathogenic. Found in alveolar suppuration and pulmonary gangrene.	1	?	2	
33	27	Veillonella gazogenes var. gingivalis MURRAY <i>Micrococcus gingivalis</i> , <i>Veillonella alcalescens</i> var. <i>gingivalis</i>	–	obligate anaerobe	Mouth cavity, also intestine	?	1	?	2	

See pages 169-171	See pages 172-178	Name Synonyms	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. application of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) - continued								
33	28	Veillonella gazogenes var. <i>minutissima</i> MURRAY <i>Micrococcus minutissimus</i> , <i>Veillonella alcalescens</i> var. <i>minutissima</i>	-	obligate anaerobe	Mouth-cavity	? Isolated from mixed-infected aphthous ulcers of the mucosa of the mouth.	1	?	2	
33	29	Veillonella gazogenes var. <i>syzygios</i> MURRAY <i>Micrococcus syzygios</i> , <i>Micrococcus syzygios scarlatinae</i> , <i>Syzygococcus scarlatinae</i> , <i>Veillonella alcalescens</i> var. <i>syzygios</i>	-	obligate anaerobe	Mouth-cavity	Found in mouth-cavity of up to 30% of healthy subjects and up to 100% of scarlet fever patients.	1	?	2	
34	30	Diplococcus pneumoniae WEICHSELBAUM <i>Bacterium pneumoniae</i> , coccus lancéolé, <i>Diplococcus lanceolatus capsulatus</i> , diplocoque, <i>Micrococcus pasteurii</i> , <i>Micrococcus pneumoniae crouposae</i> , <i>Micrococcus pyogenes tenuis</i> , pneumococcus, <i>Pneumococcus pneumoniae</i> , <i>Streptococcus pneumoniae</i>	+	facultative aerobe	Respiratory passages	Normally saprophytic; when pathogenic, cause of various infections: lobar pneumonia (90% of cases), bronchitis, bronchial pneumonia, conjunctivitis, otitis media, brain abscesses, meningitis, endocarditis, etc.	1	3	2	If a mixed infection is suspected in pneumonia, then primarily oxytetracyclin or chlorotetracyclin or a combination of the latter with penicillin. -Tetracyclins + penicillin: antagonists in pneumococcal meningitis ¹ .
34	31	Diplococcus paleopneumoniae PRÉVOT	+	obligate anaerobe	Mouth and pharynx	Isolated in cases of pleuropneumonia, from a bone abscess.	1?	3?	2?	31-33: There are no data to be found in the literature on the susceptibility of these diplococci to antibiotics. The same susceptibility as for the pneumococci has therefore been indicated. the question mark indicating that the figures are uncertain.
34	32	Diplococcus plagarumbelli PRÉVOT	+	obligate anaerobe	Septic wounds	Pathogenicity uncertain. Isolated from septic war wounds.	1?	3?	2?	
34	33	Diplococcus constellatus PRÉVOT	+	obligate anaerobe	Digestive tract, esp. appendix, tonsils	Isolated in chronic cryptic tonsillitis and acute appendicitis.	1?	3?	2?	
35	34	Streptococcus pyogenes ROSENBACH <i>Micrococcus erysipelatis</i> , <i>Micrococcus scarlatinae</i> , <i>Staphylococcus erysipelatos</i> , <i>Streptococcus erysipelatos</i> , <i>Streptococcus longus haemolyticus</i> , <i>Streptococcus longus pathogenes seu erysipelatos</i> , <i>Streptococcus puerperalis</i> , <i>Streptococcus pyogenes</i> var. <i>scarlatinae</i> , <i>Streptococcus scarlatinae</i> , streptocoque	+	facultative anaerobe, on blood agar: haemolytic (β-haemolysis), LANCEFIELD group A	Respiratory passages, dust in hospitals, occasionally in cow's udder and milk infected by human agency	Pathogen of scarlet fever, most frequent cause of bronchopneumonia in influenza and measles, frequent cause of secondary infections in diphtheria and tuberculosis, frequent cause of wound infections, erysipelas, acute tonsillitis, otitis media, and puerperal infections. Contaminated milk has already been responsible for severe angina and scarlet fever epidemics. Plays an important but still unexplained role in the aetiology of rheumatic fever with and without articular symptoms (cf. THOMAS, L., (edit.), <i>Rheumatic Fever, A Symposium</i> , Minneapolis, 1952).	1	2	2	Haemolytic streptococci: inflammations due to haemolytic streptococci are of a phlegmonous and diffuse character and are accompanied by necrosis of the tissues rather than by suppuration, in contrast to the circumscribed purulent lesions caused by staphylococci. Inflammations caused by haemolytic streptococci are generally acute in contrast to the chronic or subacute infections due to non-haemolytic or viridans streptococci. -Tetracyclins or chloramphenicol + penicillin or streptomycin: antagonists.
35	35	Streptococcus equisimilis FROST et ENGELBRECHT	+	facultative anaerobe, on blood agar: haemolytic (β-haemolysis), LANCEFIELD group C	Upper respiratory passages, vagina	See above.	1	2	2	See above.

¹) LEPPER and DOWLING, *Arch. intern. Med.*, **88**, 489, 1951.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name Synonyms	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. application of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) - continued								
35	36	Streptococcus salivarius ANDREWES et HORDER <i>Streptococcus cardio-arthritis</i>	+	facultative anaerobe, on blood agar: indifferent (γ -haemolysis). No group antigen	Mouth, nasal and pharyngeal cavities	Isolated from saliva and sputum in various lung infections, from root abscesses of teeth and carious dental lesions. See remarks.	1	0	2	Non-haemolytic (γ-haemolysis) and viridans (α-haemolysis) streptococci: These streptococci are frequently the cause of infections of the tonsils, sinus, middle ear, teeth, gallbladder and appendix. In contrast to those caused by the haemolytic streptococci the infections are of a more subacute and chronic nature and are frequently overlooked. Herein lies the reason for the dominating role played by the non-haemolytic and viridans streptococci in focal infections and in sub-acute endocarditis.
35	37	Streptococcus mitis ANDREWES et HORDER <i>Streptococcus mitior</i> seu <i>viridans</i> , <i>Streptococcus mitis</i> seu <i>viridans</i>	+	facultative anaerobe, on blood agar: green zone (α -haemolysis). No group antigen	Mouth, nasal and pharyngeal cavities	Isolated from saliva and sputum in various lung infections, from pus from the upper respiratory passages, from blood and various organs in subacute endocarditis. See remarks under 36.	1	2	2	
35	38	Streptococcus faecalis ANDREWES et HORDER <i>Diplococcus enterococcus</i> , <i>Enterococcus</i> , <i>Enterococcus proteiformis</i> , entérocoque, <i>Streptococcus ovalis</i> , <i>Streptococcus proteiformis</i>	+	facultative anaerobe, on blood agar: green zone (α -haemolysis). LANCEFIELD group D	Milk and milk products, intestinal tract	Generally non-pathogenic intestinal saprophyte. Isolated from dental granulomas, from blood in acute endocarditis. Penicillin + streptomycin: synergic action in endocarditis ¹ . See remarks under 36.	2	0	1	
35	39	Streptococcus liquefaciens STERNBERG emend. ORLA-JENSEN <i>Bacillus g�ntheri</i> , bact�ries productrices d'acide et de pr�sure, <i>Caseococcus</i> , <i>Coccus acidoproteolyticus casei</i> , <i>Mammococcus</i> , <i>Micrococcus casei amari</i> , <i>Streptococcus apis</i> , <i>Streptococcus coli gracilis</i> , <i>Streptococcus gracilis</i>	+	facultative anaerobe, on blood agar: no haemolysis or green zone (α -haemolysis). LANCEFIELD group D	Dairy products and other food-stuffs, plants, faeces, vagina	Isolated from blood in acute endocarditis. See remarks under 36.	2	0	1	
35	40	Streptococcus anaerobius KR�NIG emend. NATVIG	+	obligate anaerobe, gas-former	Human and animal body cavities, esp. vagina, intestinal tract	Can penetrate into all tissues. Isolated in cases of moist gangrene, in pleurisy, in appendicitis, from war wounds, from uterus, lochia and blood in puerperal fever.	2	0	1	
35	41	Streptococcus foetidus (VEILLON) PR�VOT <i>Micrococcus foetidus</i>	+	obligate anaerobe, gas-former	Human and animal mouth, intestinal tract and vagina	Isolated in cases of pulmonary gangrene, LUDWIG's angina, perinephritic phlegmons, appendicitis, from foetid pus from glands of BARTHOLIN.	2	0	1	
35	42	Streptococcus putridus SCHOTTM�LLER emend. PR�VOT <i>Streptococcus putrificus</i>	+	obligate anaerobe, gas-former, blackens blood agar	Mouth, intestinal tract, esp. vagina	Isolated from foetid lochia, from blood in puerperal fever, in cases of gangrenous appendicitis, pulmonary gangrene and gas gangrene, from war wounds, in osteomyelitis.	2	0	1	
35	43	Streptococcus micros PR�VOT <i>Streptococcus anaerobius micros</i>	+	obligate anaerobe, non-haemolytic	Mouth and intestinal tract	Isolated in cases of pulmonary gangrene, from lochia and uterus in puerperal sepsis, in appendicitis.	2	0	1	
35	44	Streptococcus intermedius PR�VOT	+	obligate anaerobe, on blood agar indifferent or slight green zone	Respiratory passages, intestinal tract, vagina	From lochia and uterus in puerperal sepsis, in cases of pulmonary gangrene, pleurisy, bronchiectasis, appendicitis.	2	0	1	

¹) CATES et al., *Brit. med. J.*, 1, 653, 1951.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. appli- cation of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
35	45	Bacteria (Schizomycetes) - continued Streptococcus evolutus PRÉVOT	+	initially obligate anaerobe, becoming facultative anaerobe	Mouth, respiratory passages, vagina	Isolated from skin abscesses and in appendicitis.	2	0	1	
37	46	Lactobacillus acidophilus (MORO) HOLLAND <i>Bacillus acidophilus</i> MORO, BOAS-OPPLER bacillus, <i>Plotomobacterium acidophilum</i> , <i>Thermobacterium intestinale</i>	+	micro-aerophil	Intestinal content of bottle-fed infants	Non-pathogenic.	0	0	1	When administered orally.
37	47	Lactobacillus bifidus (TISSIER) HOLLAND <i>Actinomyces bifidus</i> , <i>Bacillus bifidus</i> , <i>Bacteroides bifidus</i> , <i>Cohnistreptothrix bifidus</i> , <i>Nocardia bifida</i>	+	obligate anaerobe in young cultures, becoming micro-aerophil	Intestinal contents of breast-fed infants, to lesser extent in intestinal contents of bottle-fed infants	Non-pathogenic	0	0	1	When administered orally.
42	48	Corynebacterium diphtheriae* (FLÜGGE) LEHMANN et NEUMANN <i>Bacillus diphtheriae</i> , <i>Bacterium diphtheriae</i> , KLEBS-LOEFFLER bacillus, <i>Microsporon diphthericum</i> , <i>Pacinia loeffleri</i>	+	facultative aerobe	In mucosa of nose, pharynx, larynx and trachea of diphtheria patients, from infected superficial wounds, but also in nose and pharynx of apparently healthy subjects.	Pathogen of diphtheria, effects due solely to exotoxin secreted (neurotropic).—3 types of diphtheria bacillus: <i>gravis</i> , <i>mitis</i> , <i>intermedius</i> , with clinical pictures not always corresponding owing to the disturbing effects of other pathogens (e.g. haemolytic streptococci).	Antitoxin! 2	0	0	Penicillin is effective against <i>C. diphtheriae</i> only in very large doses (up to 1 million I.U. per day and more). See footnote*.

* Diphtheria and antibiotics

The diphtheria bacillus is about 100 times less sensitive to penicillin than, for example, the streptococci. The penicillin sensitivity *in vitro* varies between 0.004 and 1.0 I.U./ml^{1,2}, the *gravis* type as a rule being the most sensitive and the *mitis* type showing the greatest variation in sensitivity. Such concentrations cannot be attained *in vivo* with the usual dosage and this is probably the reason why some authors state that penicillin treatment is ineffective in diphtheria^{3,4}. The minimal effective dose, irrespective of age, should amount to 100,000 I.U. every three hours⁵. In the case of depot-penicillin the total daily dosage should be spread regularly over the day in groups of several simultaneous injections in order to attain a sufficiently high blood level.

Since the symptoms of diphtheria are caused only by the toxin, clinical diagnosis of diphtheria is in practice evidence that production of the toxin is already taking place. The earliest possible administration of antitoxin in sufficient quantity is therefore still the mainstay of the treatment of diphtheria. This is amply sufficient in mild cases and the use of penicillin is superfluous.

In moderate and severe cases on the other hand, where the intoxication appears to be serious, or where there is dangerous spreading of the local tissue changes with risk of stenosis, or where secondary pathogens are suspected, or again where medical

treatment has been delayed, an energetic antibiotic treatment in addition to serum therapy is absolutely indicated^{1,2,6-13}. The toxic symptoms usually react promptly, the pseudomembranes disappear more quickly, throat swabs show a more rapid fall in diphtheria bacilli, and the duration of the disease is shorter.

Diphtheria carriers should first of all be treated by local administration, which yields good results (solutions of 1000 I.U./ml as spray, gargle, etc. according to localization). If the local treatment does not suffice it should be supplemented by parenteral administration (*large doses*). Parenteral treatment alone does not appear to be so successful as local. In many cases a focal disinfection (tonsillectomy) is also necessary^{5,8,9,14,15}.

The significance of mixed bacterial flora for the severity and course of the disease has not yet been fully explained. It seems clear that haemolytic streptococci can increase diphtheria toxicity in that they cause an increase in tissue permeability and thus promote resorption and distribution of the toxin^{16,17}. An influence has also been ascribed to other species of bacteria, such as haemolytic staphylococci¹⁸ and anaerobes¹⁹. Penicillin is suitable for the treatment of streptococcal and staphylococcal mixed infections (carbomycin or erythromycin for resistant staphylococci), but should be replaced by one of the tetracyclins for anaerobes, against which it is ineffective.

¹) LONG, D. A., *Brit. med. J.*, **1**, 773, 1946. ²) CRUICKSHANK et al., *Lancet*, **2**, 517, 1948. ³) HEWITT, *Brit. J. exp. Path.*, **29**, 289, 1948. ⁴) BRUYN et al., *Amer. J. med. Sci.*, **219**, 408, 1950. ⁵) FLOREY, M. E., *The Clinical Application of Antibiotics* (Penicillin), Oxford University Press, 1952. ⁶) LONG, D. A., *Brit. med. J.*, **1**, 884, 1947. ⁷) DE et al., *Brit. med. J.*, **1**, 376, 1947. ⁸) WEINSTEIN, L., *Amer. J. med. Sci.*, **213**, 308, 1947. ⁹) KARELITZ, S., *Bull. U. S. Army med. Dep.*, **7**, 257, 1947. ¹⁰) BIXBY, E. W., *Amer. J. med. Sci.*, **215**, 509, 1948. ¹¹) SCHNEIDER, R., *Ärztl. Wschr.*, **6**, 1112, 1951. ¹²) VORLAENDER and KERP, *Klin. Wschr.*, **30**, 982, 1952. ¹³) SCHNEIDER, R., *Ärztl. Wschr.*, **8**, 223, 1953 (Penicillin plus Streptomycin). ¹⁴) CRAWFORD, J. D., *New Engl. J. Med.*, **239**, 220, 1948. ¹⁵) OBERG, G., *Acta paediat.*, **37**, 204, 1949. ¹⁶) UPDYKE and FROBISHER, *J. Bact.*, **54**, 619, 1947. ¹⁷) KOCH and ROEMER, *Klin. Wschr.*, **30**, 654, 1952. ¹⁸) BERGER, U., *Schweiz. med. Wschr.*, **81**, 130, 1951. ¹⁹) DOSKOČIL, A., *Zbl. Bakt.*, **146**, 350, 1941.

See pages 169-171	See pages 172-178	Name Synonyms	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. application of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) - continued								
42	49	Corynebacterium acnes (GILCHRIST) EBERSON <i>Actinomyces acnes</i> , <i>Bacillus acnes</i> , <i>Fusiformis acnes</i> , <i>Propionibacterium acnes</i>	+	microaerophil to anaerobe	Sebaceous glands, hair follicles	Isolated from acne pustules.	1?	0	0	
43	50	Listeria monocytogenes (MURRAY et al.) PIRIE <i>Bacillus monocytogenes</i> , <i>Bacterium monocytogenes</i> , <i>Corynebacterium parvulum</i> , <i>Listerella hepatolytica</i> , <i>Listerella monocytogenes hominis</i>	+	facultative aerobe	In patients	According to NYFELDT, <i>Folia haemat.</i> , 47 , 1932, pathogen of infectious mononucleosis.	?	?	1	Cf. ¹ .
44	51	Erysipelothrix rhusiopathiae (MIGULA) WINSLOW et al. <i>Actinomyces thuillieri</i> , <i>bacille du rouget</i> , <i>Bacillus erysipelatos suis</i> , <i>Bacillus rhusiopathiae suis</i> , <i>Bacillus ruboris suis</i> , <i>Bacillus thuillieri</i> , <i>Bacterium erysipelatos suum</i> , <i>Bacterium rhusiopathiae suis</i> , <i>Erysipelothrix erysipelatos suis</i> , <i>Mycobacterium rhusiopathiae</i> , <i>Nocardia thuillieri</i> , <i>Pasteurella thuillieri</i>	+	micro-aerophil		Pathogen of swine erysipelas and erysipeloid in man. Incubation time ca. 2 days. Risk of infection particularly high for persons handling infected meat. Fish can also be infected (possible post-mortem infection).	1	2	2	Penicillin + streptomycin have a synergic action. In contrast to swine erysipelas, erysipeloid in man is a localized infection, predominantly on the hand (thumb, index finger, back). It can have the appearance of a paronychia and is often mistaken for it. Duration (without antibiotics) 2-3 weeks. Intermittent fever can also occur, and erysipeloid septicaemia is also mentioned in the literature ² . For a review, see ³ .
44	52	Erysipelothrix erysipeloidis (LEHMANN et NEUMANN) ROSENBACH <i>Actinomyces erysipeloidis</i> , <i>Actinomyces rosenbachii</i> , <i>Babesia erysipeloides</i> , <i>Bacterium erysipeloidis</i> , <i>Cladothrix des Erythema migrans</i> , <i>Discomyces rosenbachi</i> , <i>Nocardia rosenbachi</i> , <i>Oospora erysipeloidis</i> , <i>Oospora rosenbachi</i> , <i>Streptothrix erysipeloides</i> , <i>Streptothrix rosenbachii</i>	+	micro-aerophil		Isolated from cases of human erysipeloid.	1	2	2	See above (51).
45	53	Alcaligenes faecalis CASTELLANI et CHALMERS <i>Bacillus alcaligenes</i> , <i>Bacillus faecalis alcaligenes</i> , <i>Bacterium faecalisalcaligenes</i> , <i>Vibrio alcaligenes</i>	-	facultative aerobe	Intestinal tract	Regarded as non-pathogenic. Isolated from abscesses connected with the intestinal tract, occasionally from the blood.	?	?	?	
48	54	Escherichia coli (MIGULA) CASTELLANI et CHALMERS <i>Aerobacter coli</i> , <i>Bacillus coli communis</i> , <i>Bacillus coli verus</i> , <i>Bacillus escherichii</i> , <i>Bacterium coli commune</i> , <i>colibacillus</i> , <i>Colobactrum coli</i>	-	facultative aerobe	Intestinal tract	Normal intestinal saprophyte of man and animals, widely distributed in nature. Frequent cause of infections of the urogenital system (up to 30% of cases) (paranephritic abscesses, pyelonephritis, cystitis), cholecystitis and peritonitis.	0	2	1	In the death struggle <i>E. coli</i> often penetrates into the tissues and blood stream.
49	55	Aerobacter aerogenes (KRUSE) BEIJERINCK <i>Bacillus aerogenes</i> , <i>Bacillus lactantium</i> , <i>Bacillus lactis aerogenes</i> , <i>Bacterium aerogenes</i> , <i>Bacterium lactis aerogenes</i> , <i>Colobactrum aerogenes</i> , <i>Encapsulatus lactis-aerogenes</i>	-	facultative aerobe	On plants, in variable quantities in intestinal tract of man and animals. Widely distributed in nature.	Normal intestinal saprophyte. Frequent cause of infections of the urogenital system (up to 40% of cases). Has also been isolated from blood.	0	2	1	

¹) BENNET, I. L., *Antibiot. and Chemother.*, **2**, 142, 1952. ²) LODENKÄMPFER and NICKEL, *Ärztl. Wschr.*, **8**, 697, 1953. ³) BINGOLD and TRUMMERT, *Ärztl. Wschr.*, **7**, 593, 1952.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. appli- cation of antibiotics			Remarks
			Gram's staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) - continued								
49	56	Aerobacter cloacae (JORDAN) BERGEY et al. <i>Bacillus cloacae</i> , <i>Bacillus lactis cloacae</i> , <i>Bacterium cloacae</i> , <i>Cloaca cloacae</i>	-	facultative aerobe, produces faecal odour	Human and animal faeces, cloaca, water, soil	Normal intestinal saprophyte. No information in the literature on possible pathogenicity.	0	2	1	
50	57	Klebsiella pneumoniae (SCHROETER) TREVISAN <i>Bacillus friedlanderi</i> , <i>Bacillus mucosus-capsulatus</i> , <i>Bacillus pneumoniae</i> , <i>Bacterium friedlander</i> , <i>Bacterium pneumoniae crouposae</i> , <i>Bacterium pneumonicum</i> , <i>Coccobacillus friedlanderi</i> , <i>Encapsulatus pneumoniae</i> , FRIEDLANDER's bacillus, <i>Hyalococcus pneumoniae</i> , <i>Klebsiella crouposa</i> , <i>Klebsiella friedlanderi</i> , <i>Protens pneumoniae</i>	-	facultative aerobe	In patients	Causative organism of ca. 5% of cases of lobar and lobular pneumonia, which are usually more severe than those due to <i>Diplococcus pneumoniae</i> . Also causes tonsillitis (esp. in children), meningitis and inflammation of the sinus and middle ear.	0	2	1	Antibiotics of choice for all capsulated bacteria (57, 58, 59, 60): tetracyclins ¹ . Cf. ² and ³ . In the case of infections caused by <i>Klebsiellae</i> the tetracyclins or chloramphenicol are antagonistic to penicillin or streptomycin ⁴ .
50	58	Klebsiella granulomatis (ARAGAO et VIANNA) BERGEY et al. <i>Calymmatobacterium granulomatis</i>	-	facultative anaerobe		Isolated in cases of granuloma inguinale but very probably as secondary infection. Aetiological connection quite uncertain.	0	2	1	Cf. (57) and <i>Donovania</i> (87).
50	59	Klebsiella ozaenae (ABEL) BERGEY et al. <i>Bacillus capsulatus-mucosus</i> , <i>Bacillus mucosus ozaenae</i> , <i>Bacillus ozaenae</i> , <i>Bacterium mucosum-capsulatum</i> , <i>Bacterium mucosus ozaena</i> , <i>Encapsulata ozaenae</i>	-	facultative anaerobe		Isolated in cases of ozaena. Aetiological connection very doubtful.	0	2	1	Cf. (57).
50	60	Klebsiella rhinoscleromatis TREVISAN <i>Bacillus rhinoscleromatis</i> , <i>Bacterium nasalis</i> , <i>Bacterium rhinoscleromatis</i> , Rhinosclerom-bazillus von FRISCH	-	facultative anaerobe		Isolated in cases of rhinoscleroma. Aetiological connection uncertain.	0	2	1	Cf. (57).
51	61	Paracolobactrum aerogenoides BORMAN, STUART et WHEELER <i>Para-aerogenes</i> , <i>Paracolonbacillus</i>	-	facultative aerobe	Surface water, soil, intestinal tract of man and animals	Saprophyte. In isolated cases cause of enteritis and infections of the urogenital tract.	0	2	1	Characteristics similar to <i>Aerobacter aerogenes</i> .
51	62	Paracolobactrum intermedium BORMAN, STUART et WEBER <i>Paracolonbacillus</i> , <i>Para-freundii</i>	-	facultative aerobe	See above (61)	See above (61).	0	2	1	Characteristics similar to <i>Escherichia freundii</i> , which in turn resembles <i>Escherichia coli</i> .
51	63	Paracolobactrum coliforme BORMAN, STUART et WHEELER <i>Bacillus para-colon</i> , <i>Para-coli</i>	-	facultative aerobe	See above (61)	See above (61).	0	2	1	Characteristics similar to <i>Escherichia coli</i> .
54	64	Proteus vulgaris HAUSER <i>Bacillus protens vulgaris</i> , <i>Bacterium protens anindologenes</i> , <i>Bacterium protens vulgaris</i> , <i>Bacterium vulgare</i>	-	facultative aerobe, produces foetid odour	Regularly on putrescent material, in sewage, intestinal tract	Usually non-pathogenic; when pathogenic, usually in combination with other organisms, cause of enteritis (contamination of food-stuffs, in these cases also identifiable in blood), otitis media, peritonitis, cystitis, pyelitis, and other inflammations.	Neomycin B 0 2 0			Antibiotic of choice: neomycin B . The serum of patients with typhus causes agglutination of the OX 19 strain of <i>Proteus</i> (although the latter has no aetiological connection with this disease). This property is used in the diagnosis of typhus (WEIL-FELIX reaction).

¹) LEGLER, F., *Zbl. Bakt.*, **159**, 101, 1952. ²) NATARO et al., *J. Amer. med. Ass.*, **144**, 12, 1950. ³) WYLIE and KIRSCHNER, *Amer. Rev. Tuberc.*, **61**, 465, 1950. ⁴) DOWLING et al., *J. Amer. med. Ass.*, **151**, 813, 1953.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. appli- cation of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) - continued								
54	65	Proteus mirabilis HAUSER <i>Bacillus mirabilis, Bacillus proteus mirabilis, Bacillus pseudoramossus</i>	-	facultative aerobe	See previous page (64)	See previous page (64).	Neomycin B 0 2 0			Antibiotic of choice: neomycin B.
54	66	Proteus morganii (WINSLOW et al.) RAUSS <i>Bacillus morgani, Bacterium metacoli, Bacterium morgani, Escherichia morgani, Morganella morganii, MORGAN's bacillus No. 1, Salmonella morgani</i>	-	facultative aerobe	See previous page (64)	See previous page (64). Also isolated from faeces in summer diar- rhoea.	0	2	0	As above (65).
55	67	Salmonella paratyphi (KAYSER) CASTELLANI et CHALMERS <i>Bacillus paratyphi, Bacillus paratyphosus A, Bacterium para-typhi, Bacterium paratyphosum A, Salmonella paratyphi A</i>	-	facultative aerobe	Intestinal contents of patients, contaminated water and food	Obligate pathogen of man. Causes enteritis, paratyphoid A clini- cally similar to typhoid.	Chloram- phenicol 0 3 2			Salmonella (67-75): Over 150 serologically different <i>Salmonella</i> have been distinguished up to now by their antigenic characteristics. These antigenic types have been given various names, after patients, hospitals, localities, etc., e. g. <i>Salmonella</i> sp. type Stanley, type London, etc. For clas- sification, see ¹ and ² .
55	68	Salmonella schottmuelleri (WINSLOW et al.) BERGEY et al. <i>Bacillus paratyphi alcaligenes, Bacillus paratyphosus B, Bacillus schottmülleri, Bacterium paratyphosum B, Bacterium schottmülleri, Salmonella paratyphi B</i>	-	facultative aerobe	See above (67)	Obligate pathogen of man, to a lesser extent of animals. Like para- typhoid A, paratyphoid B is clinically similar to typhoid, although there are differences due to the greater serological inhomogeneity of the paratyphoid B group. Clinically, the following types may be distin- guished: a dysentery type, a nephritic type, a rheumatic type, an in- fluenza type. Para- typhoid B infections can also take on the appearance of meat- poisoning.	Chloram- phenicol 0 3 2			
55	69	Salmonella typhimurium (LOEFFLER) CASTELLANI et CHALMERS <i>Bacillus aertrycke, Bacillus cho-lera-caviae, Bacillus enteritidis B, type murium, Bacillus murium, Bacillus para-aertrycke, Bacillus pestis-caviae, Bacillus typhi mu-rium, Bacterium aertrycke, Bac-terium enteritidis breslau, Bac-terium psittacosis, Bacterium typhi-murium, Pasteurella pestis-caviae, Salmonella anatum var. aertrycke, Salmonella breslau, Salmonella psittacosis</i>	-	facultative aerobe	In animal and human patients	Obligate pathogen of all warm-blooded ani- mals including man. In man the infection has the appearance of food- poisoning.	Chloram- phenicol 0 3 2			A further variety of <i>S. typhimurium</i> can be dis- tinguished: <i>Salmonella typhimurium</i> , type Binns (<i>Bacillus paratyphosus B</i> , Binns type; <i>Salmonella aertrycke</i> var. Storrs; <i>Salmonella typhimurium</i> var. Copenhagen).
55	70	Salmonella hirschfeldii WELDIN <i>Bacillus erzincjan, Bacillus para-typhosus C, Bacterium hirschfeldii, Salmonella paratyphi C, Salmonella paratyphosus C</i>	-	facultative aerobe	In patients	Causes enteritis, obli- gate pathogen.	Chloram- phenicol 0 3 2			

¹) KAUFFMANN, *Acta path. microbiol. scand.*, 22, 144, 1945. ²) BREED et al., *Bergey's Manual of Determinative Bacteriology*, New York, 1948.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name Synonyms	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. appli- cation of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) – continued								
55	71	Salmonella choleraesuis (SMITH) WELDIN <i>Bacillus cholerae-suis</i> , <i>Bacillus salmoni</i> , <i>Bacillus suipestifer</i> , <i>Bacillus suis</i> , <i>Bacterium cholerae-suis</i> , <i>Bacterium intestinale suis</i> , <i>Bacterium suipestifer</i> , <i>Salmonella suipestifer</i>	–	facultative aerobe	In swine as secondary agent of (virus-) hog cholera	Only in swine regularly pathogenic. In man it occasionally causes acute gastroenteritis and enteric fever.	Chloram-phenicol 0 3 2			A further variety of <i>S. choleraesuis</i> can be distinguished: <i>Salmonella choleraesuis</i> var. KUNZEN-DORF (the European <i>S. suipestifer</i> of many au-thors).
55	72	Salmonella typhosa (ZOPF) WHITE <i>Acystia typhi</i> , <i>Bacillus typhi abdominalis</i> , <i>Bacillus typhosus</i> , <i>Bacterium typhi</i> , <i>Bacterium typhosum</i> , EBERTH's bacillus, <i>Eberthella typhosa</i> , <i>Eberthus typhosus</i> , <i>Salmonella typhi</i> , <i>Vi-brio typhosus</i>	–	facultative aerobe	In patients, faeces, contaminated water	Pathogen of human typhoid fever, only pathogenic for animals when parenterally ad-ministered.	Chloram-phenicol 0 3 2			In addition, ACTH, hydrocortisone or corti-sone ¹ .
55	73	Salmonella enteritidis (GÄRTNER) CASTELLANI et CHALMERS <i>Bacillus enteritidis</i> , <i>Bacillus gaertner</i> , <i>Bacterium enteritidis</i> , GÄRTNER's bacillus, <i>Klebsiella enteritidis</i>	–	facultative aerobe	Widely distributed in man and animals (sick and healthy carriers)	Causes enteritis, mainly in meat-poisoning.	Chloram-phenicol 0 3 2			
55	74	Salmonella pullorum (RETTGER) BERGEY et al. <i>Bacillus pullorum</i> , <i>Bacterium pullorum</i>	–	facultative aerobe	In affected poultry and its excrement	Pathogenic for (young) poultry and other birds, warm-blooded animals including man. Cause of white diarrhoea of chicks. Infects the ova-ries and eggs of adult birds.	Chloram-phenicol 0 3 2			Ducks' eggs are often infected, also by <i>S. enteritidis</i> , and should be eaten therefore only when well cooked. Many enteritis epi-demics (in institutions) have already been caused by scrambled egg and mayonnaise from ducks' eggs.
55	75	Salmonella anatis (RETTGER et SCOVILLE) BERGEY et al. <i>Bacterium anatis</i> , <i>Bacterium anatum</i> , <i>Escherichia anata</i> , <i>Sal-monella anatum</i>	–	facultative aerobe	Widely distributed in domestic animals and man	Often found with <i>S. typhimurium</i> . Causes en-teritis.	Chloram-phenicol 0 3 2			
56	76	Shigella dysenteriae (SHIGA) CASTELLANI et CHALMERS <i>Bacillus dysenteriae</i> , <i>Bacillus dys-entericus</i> , <i>Bacillus japonicus</i> , <i>Bacillus shigae</i> , <i>Bacterium dys-enteriae</i> , <i>Bacterium shigae</i> , <i>Eberthella dysenteriae</i>	–	facultative aerobe	In patients, contaminated water, food, etc.	Pathogen of dysentery.	Chloram-phenicol 0 3 2			Mainly in tropical East Asia.
56	77	Shigella ambigua (ANDREWES) WELDIN <i>Bacillus ambiguus</i> , <i>Bacillus dys-enteriae</i> SCHMITZ, <i>Bacterium ambiguum</i> , <i>Bacterium schmitzii</i> , <i>Eberthella ambigua</i> , SCHMITZ's bacillus, <i>Shigella schmitzii</i>	–	facultative aerobe	See above (76)	See above (76).	Chloram-phenicol 0 3 2			Predominantly in the east.
56	78	Shigella gintottensis (CASTELLANI) HAUDUROY et al. <i>Bacillus gintottensis</i> , <i>Castellanus gintottensis</i> , <i>Lankoides gintot-tensis</i>	–	facultative aerobe	See above (76)	See above (76).	Chloram-phenicol 0 3 2			
56	79	Shigella paradysenteriae (COLLINS) WELDIN <i>Bacillus dysenteriae</i> FLEXNER, <i>Bacillus flexneri</i> , <i>Bacillus para-dysenteriae</i> , <i>Bacterium flexneri</i> , <i>Bacterium paradysenteriae</i> , <i>Eber-thella flexneri</i> , <i>Eberthella para-dysenteriae</i> , <i>Shigella flexneri</i>	–	facultative aerobe	See above (76)	See above (76).	Chloram-phenicol 0 3 2			Mainly in USA. The following types of <i>Sh. paradysenteriae</i> can be distinguished serologi-cally: Types FLEXNER I–VI (FLEXNER VI = Type Newcastle and Type Manchester) and Types BOYD I–III.

¹) DURAND and RENOUX, *Sem. Hôp. Paris*, 29, 2555, 1953.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name Synonyms	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. appli- cation of antibiotics			Remarks
			Gram's staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) - continued								
56	80	Shigella alkalescens (ANDREWES) WELDIN <i>Bacillus alkalescens</i> , <i>Bacterium alkalescens</i> , <i>Eberthella alkalescens</i> , <i>Proshigella alkalescens</i>	-	facultative aerobe	In patients and their excrement; contaminated food, water	Causes dysentery, also infections of the urogenital tract.	Chloramphenicol 0	3	2	
56	81	Shigella sonnei (LEVINE) WELDIN <i>Bacille de SONNE</i> , <i>Bacillus ceylonensis</i> , <i>Bacillus dispar</i> , <i>Bacillus dysenteriae</i> SONNE, <i>Bacterium sonnei</i> , <i>Castellanus kruse-castellani</i> , <i>Proshigella sonnei</i> , <i>Pseudodysenteriebazillus</i> E, KRUSE, <i>Shigella paradysenteriae</i> var. <i>sonnei</i>	-	facultative aerobe	See above (80)	Cause of mild dysentery, summer diarrhoea of children.	Chloramphenicol 0	3	2	Distributed throughout the world.
56	82	Shigella ceylonensis (CASTELLANI) WELDIN <i>Bacillus ceylonensis</i> B, <i>Bacillus dispar</i> , <i>Castellanus castellanii</i> , <i>Eberthella dispar</i> , <i>Lankoides ceylonensis</i> B	-	facultative aerobe	See above (80)	Causes dysentery.	Chloramphenicol 0	3	2	Tropics.
57	83	Pasteurella pestis* (LEHMANN et NEUJANN) HOLLAND <i>Bacillus pestis bubonicae</i> , <i>Bacterium pestis bubonicae</i> , <i>Coccobacillus yersini</i> , <i>Eucystia pestis</i>	-	facultative aerobe	Infected rodents, esp. rats; rat fleas, man	Pathogen of plague (pneumonic and bubonic plague). Pathogenic for all rodents and man.	0	2	1	Antibiotics of choice: tetracyclins. See footnote*.
57	84	Pasteurella tularensis (MCCOY et CHAPIN) BERGEY et al. <i>Bacillus tularense</i> , <i>Bacterium tularense</i> , <i>Brucella tularensis</i> , <i>Coccobacterium tularense</i>	-	aerobe	In over 30 species of wild animals, transmitted by blood-sucking insects, also via water	Pathogen of tularaemia (buboes and tissue necroses), mainly in liver, lymphatic glands and blood.	0	2	1	Distributed throughout the world.
58	85	Malleomyces mallei (ZOPF) PRIBRAM <i>Actinobacillus mallei</i> , <i>Bacille de la morve</i> , <i>Bacillus mallei</i> , <i>Bacillus ozaenae</i> , <i>Bacterium mallei</i> , <i>Brucella mallei</i> , <i>Cladascus mallei</i> , <i>Corynebacterium mallei</i> , <i>Mycobacterium mallei</i> , <i>Loefflerella mallei</i> , <i>Pfeifferella mallei</i> , <i>Sclerothrix mallei</i>	-	aerobe, facultative anaerobe	In affected horses and man	Pathogen of horse glanders, also pathogenic for man.	?	1	?	
59	86	Actinobacillus lignieresii BRUMPT <i>Bacillus lignieri</i> , <i>Bacterium purifaciens</i> , <i>Discomyces lignieresii</i> , <i>Nocardia lignieresii</i> , <i>Pasteurella lignieresii</i> , <i>Pasteurella purifaciens</i>	-	aerobe	In affected animals	Actinobacillosis of cows and swine (often described as actinomycosis, from which it differs). Affects man in isolated cases.	?	?	?	
60	87	Donovania granulomatis ANDERSON et al. Epithelial cell parasites, DONOVAN; DONOVAN bodies, DIENST et al.; DONOVAN organism, ANDERSON et al.	-	Cultures only in living chicken embryos	In patients	Pathogen of granuloma inguinale, non-pathogenic for animals.	0	2	1	Cf. 2.

* Plague and antibiotics

Antibiotics of choice: tetracyclins (very effective, oral administration)^{1, 3}. Streptomycin is equally effective but less convenient on account of its toxicity and the unsuitability of parenteral administration in culturally undeveloped countries. The sulphonamides are also quite effective and can be applied in

practice as initial remedy, particularly for bubonic plague. If sulphonamide treatment causes no improvement or even deterioration, and in all cases of pneumonic plague, immediate treatment with antibiotics is indicated (see above, penicillin is useless). For a review, see¹.

¹) POLLITZER, R., *Bull. Wld. Hlth. Org.*, 9, 59, 1953. ²) ZISES et al., *Amer. J. Syph.*, 35, 294, 1951. ³) MCCRUMB et al., *Amer. J. Med.*, 14, 284, 1953.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. appli- cation of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) - continued								
61	88	Brucella melitensis (HUGHES) MEYER et SHAW <i>Alcaligenes melitensis, Bacillus melitensis, Bacterium melitense, Brucella melitensis</i> var. <i>melitensis</i> EVANS, <i>Micrococcus melitensis, Streptococcus melitensis</i>	-	aerobe	In affected cattle, esp. goats. Mainly prevalent in Mediterranean area	Pathogen of brucellosis (undulant fever, Malta fever, rock fever). Infectious for all domestic animals.	see remarks 0	2	1	This assessment is valid only for the application of a single antibiotic. Combinations of the tetracyclins + streptomycin give the best results. In order to avoid recidivation, treatment should extend over 3-4 weeks, 5-day periods at 2 g (30 grains)/day alternating with 5-day periods without antibiotic ^{1, 2, 3} .
61	89	Brucella abortus (SCHMIDT et WEIS) MEYER et SHAW <i>Alcaligenes abortus, Bacillus abortus, Bacterium abortivum, Bacterium abortus, Corynebacterium abortus endemici</i>	-	aerobe	In affected domestic animals, esp. cows. Mainly prevalent in central and northern Europe	Pathogen of BANG's disease (cattle) and brucellosis (man). Causes epidemic epizootic abortion in cows. Pathogenic for all domestic animals.	see remarks 0	2	1	See above (88).
61	90	Brucella suis HUDDLESON <i>Bacillus abortus suis, Brucella melitensis</i> var. <i>suis</i>	-	aerobe	In affected domestic animals, esp. swine	Pathogen of epidemic abortion in swine, brucellosis in man.	see remarks 0	2	1	See above (88).
61	91	Brucella bronchiseptica (FERRY) TOPLEY et WILSON <i>Alcaligenes bronchisepticus, Bacillus bronchicanis, Bacillus bronchisepticus, Bacterium bronchicanis, Bacterium bronchisepticus</i>	-	facultative aerobe	In affected animals	In distemper cases often the cause of secondary (frequently fatal) bronchopneumonia. Pathogenic for cats, guinea-pigs, rats, rabbits, apes, and monkeys. Also isolated cases in man (uncertain).	?	?	?	
62	92	Bacteroides fragilis (VEILLON et ZUBER) CASTELLANI et CHALMERS <i>Bacillus fragilis, Fusiformis fragilis, Ristella fragilis</i>	-	anaerobe	Intestinal tract	Isolated in acute appendicitis, pulmonary gangrene, abscesses of urogenital tract, septicaemia (bacteroidosis).	0	2	1	
62	93	Bacteroides funduliformis (HALLÉ) BERGEY et al. <i>Bacillus funduliformis, Bacillus thetoides, Spherophorus funduliformis</i>	-	anaerobe	Intestinal tract, female genitals	Infections of the urogenital tract, appendicitis, puerperal fever, otitis, pulmonary gangrene, liver abscesses, septicaemia (bacteroidosis).	0	2	1	
63	94	Fusobacterium plauti-vincenti KNORR <i>Fusiformis plauti-vincenti, Fusiformis vincenti</i>	-	anaerobe	Mouth-cavity	Together with <i>Borrelia vincentii</i> (153), cause of PLAUT-VINCENT angina.	1	3	2	
64	95	Haemophilus influenzae (LEHMANN et NEUMANN) WINSLOW et al. <i>Bacillus influenzae, Bacterium aegyptiacum, Bacterium influenzae, Coccobacillus pfeifferi, Haemophilus conjunctivitis, Haemophilus meningitidis cerebrospinalis septicaemiae, PFEIFFER's bacillus.</i>	-	facultative aerobe	Respiratory passages	Cause of acute infections of the respiratory tract, acute conjunctivitis, purulent meningitis in children (rare in adults).	0	1 see remarks	1	Plus sulphonamides. Cf. ⁴ and ⁵ . LEPPER ⁶ obtained better results in meningitis with chlorotetracyclin alone.
64	96	Haemophilus haemolyticus BERGEY et al.	-	facultative aerobe	Upper respiratory passages	Non-pathogenic.	0	3	1	
64	97	Haemophilus para-influenzae RIVERS	-	facultative aerobe	Upper respiratory passages	Usually non-pathogenic.	0	3	1	

¹) CASTANEDA and IBARRA, *Antibiot. and Chemother.*, **2**, 86, 1952. ²) HERRELL and BARBER, *Proc. Mayo Clin.*, **24**, 138, 1949. ³) HALL, W. H. *Minnesota Med.*, **36**, 460, 1953. ⁴) APPELBAUM and NELSON, *J. Amer. med. Ass.*, **143**, 715, 1950. ⁵) PRATHER and SMITH, *J. Amer. med. Ass.*, **143**, 1405, 1950. ⁶) LEPPER et al., *Amer. J. Dis. Child.*, **83**, 763, 1952.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name Synonyms	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. application of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) - continued								
64	98	Haemophilus pertussis HOLLAND Bacille de la coqueluche, <i>Bacillus pertussis</i> , <i>Bacterium tussis convulsivae</i> , BORDET-GENGOU bacillus	-	aerobe	In patients	Pathogen of whooping cough (pertussis).	2	2	1	The tetracyclins are not significantly more effective than penicillin, streptomycin or sulphonamides ¹ .
64	99	Haemophilus ducreyi (NEVEU-LEMAIRE) BERGEY et al. <i>Bacillus ulceris cancrisi</i> , <i>Bacterium ulceris cancrisi</i> , <i>Coccobacillus ducreyi</i>	-	facultative aerobe	In patients	Pathogen of chancroid.	0	3	2	
64	100	Streptobacillus moniliformis LEVADITI et al. <i>Actinomyces muris</i> , <i>Actinomyces muris ratti</i> , <i>Asterococcus muris</i> , <i>Haverhillia multiformis</i> , <i>Streptothrix ratti</i>	-	facultative aerobe	Rats and mice	Causes a form of rat-bite fever (haverhill fever, erythema arthriticum epidemicum), transmitted by rat bite and also by contaminated food, esp. milk. Cf. rat-bite fever caused by <i>Spirillum minus</i> (4).	0	1	?	
65	101	Moraxella lacunata (EYRE) LWOFF <i>Bacillus duplex</i> , <i>Bacillus lacunatus</i> , <i>Bacterium conjunctivitis</i> , <i>Diplobacillus moraxaxenfeld</i> , <i>Haemophilus duplex</i> , <i>Haemophilus lacunatus</i> , MORAX-AXENFELD bacillus	-	facultative aerobe	In patients	Pathogen of subacute angular conjunctivitis.	0	2	1	Two variants are distinguished: <i>Moraxella lacunata</i> var. <i>typica</i> and <i>Moraxella lacunata</i> var. <i>atypica</i> .
65	102	Moraxella liquefaciens comb. nov. (McNAB) <i>Bacillus duplex liquefaciens</i> , <i>Diplobacillus liquefaciens</i> , <i>Moraxella duplex liquefaciens</i> , <i>Moraxella duplex</i> var. <i>liquefaciens</i>	-	aerobe	In patients	Pathogen of conjunctivitis, also connected with ulceration of the cornea.	0	2	1	
66	103	Noguchia granulosi (NOGUCHI) OLITSKY et al.	-	aerobe, facultative anaerobe		Considered by NOGUCHI to be pathogen of human trachoma.	?	?	?	Cf. 176.
67	104	Dialister pneumosintes (OLITSKY et GATES) BERGEY et al. <i>Bacillus pneumosintes</i> , <i>Bacterium pneumosintes</i>	-	obligate anaerobe		Isolated from nasopharyngeal secretions of early-stage influenza patients. Pathogenicity uncertain.	?	?	?	
67	105	Dialister granuliformans (PAVLOVIC) BERGEY et al.	-	anaerobe to micro-aerophil	Mucosa of the respiratory passages	Isolated from the respiratory tract in influenza. Pathogenicity uncertain.	?	?	?	DE BORD ² has described a new tribe of the family <i>Parvobacteriaceae</i> : <i>Mimeae</i> , embracing the species <i>Mima polymorpha</i> , <i>Herellea vaginicola</i> and <i>Colloides anoxydana</i> .
68	106	Mima polymorpha DE BORD	-	?	Vagina	Isolated in cases of vaginitis and conjunctivitis.	0	0	1	
68	107	Herellea vaginicola DE BORD	-	?	Vagina	Isolated in cases of vaginitis and conjunctivitis.	0	0	1	
68	108	Colloides anoxydana DE BORD	-	?	Vagina	Isolated in cases of vaginitis and conjunctivitis.	0	0	1	See above (106).
71	109	Bacillus anthracis COHN emend. KOCH <i>Aplanobacter anthracis</i> , bactérie charbonneuse, <i>Bacteridium anthracis</i> , <i>Bacterium anthracis</i> , <i>Pollendera anthracis</i>	+	facultative aerobe	In affected animals and man	Pathogen of anthrax. Pathogenic for cows, sheep, swine, and occasionally for man.	1	0	1	

¹) LA BOCCETTA and DAWSON, *Amer. J. Dis. Child.*, **84**, 184, 1952. ²) DE BORD, *Iowa State Coll. J. Sci.*, **16**, 471, 1942.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name Synonyms	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. application of antibiotics			Remarks
			GRAM'S staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) - continued								
72	110	Clostridium fallax (WEINBERG et SEGUIN) BERGEY et al. Bacille A de WEINBERG et SEGUIN, <i>Bacillus fallax</i> , <i>Vallo-rillus fallax</i>	+	anaerobe, gas-former		Pathogen of gas gan-grene. Isolated from war wounds and in ap-pendicitis.	1	0	2	
72	111	Clostridium septicum (MACÉ) FORD <i>Bacillus septicus</i> , <i>Bacillus septi-cus ulceris gangraenosi</i> , <i>Bacillus parasarcophysematos</i> , <i>Bacillus tumefaciens</i> , <i>Clostridium balae-nae</i> , <i>Clostridium tumefaciens</i> , <i>Cornilia pasteurii</i> , <i>Rivoltillus vi-brion</i> , <i>Vibrio pasteurii</i> , <i>Vibrio septicus</i> , <i>Vibrion septicus</i> of PASTEUR et JOUBERT (not <i>Ba-cillus oedematis maligni</i>)	+	anaerobe, gas-former	In manured soil, intestinal tract	One of the pathogens of gas gangrene, produces a violent toxin.	1	0	2	Plus antitoxin.
72	112	Clostridium novyi (MIGULA) BERGEY et al. Bacille B de WEINBERG et SE-GUIN, <i>Bacillus novyi</i> , <i>Bacillus oedematis</i> , <i>Bacillus oedematis maligni</i> No. 2, <i>Bacillus oede-matis thermophilus</i> , <i>Bacillus thermophilus</i> , <i>Bacterium oedema-tis thermophilus</i> , <i>Clostridium oedematis</i> , <i>Clostridium thermo-philum</i> , <i>Novillus maligni</i>	+	anaerobe, gas-former	In manured soil, intestinal tract	Frequent cause of gas gangrene, pathogenic for man and animals, produces a violent toxin.	1	0	2	Plus antitoxin.
72	113	Clostridium botulinum (VAN ERMENGEM) HOLLAND <i>Bacillus botulinus</i> , <i>Emergemillus botulinus</i>	+	anaerobe	Presumably in soil	No direct pathogenic action on man. The exotoxin produced, however, is an extra-ordinarily potent nerve poison: botulism. See remarks.	Antitoxin			Most cases of botulism occur through eating preserves which have gone bad, particularly home-made preserves of beans, peas or meat served cold (ca. 80% of cases due to bean salad). <i>Cooking destroys the toxin</i> .—Administra-tion of large doses of antitoxin or sympto-matic detoxication is the sole effective treat-ment (gastric lavage is usually too late, as the toxin works slowly).
72	114	Clostridium aerofoetidum (WEINBERG et SEGUIN) BERGEY et al. Bacille D de WEINBERG et SE-GUIN, <i>Bacillus aerofoetidus</i> , <i>Se-guinillus aerofoetidus</i>	+	anaerobe, gas-former	Presumably in soil. In intestinal tract	Pathogen of gas gan-grene.	1	0	2	
72	115	Clostridium sporogenes (METCHNIKOFF) BERGEY et al. <i>Bacillus enteritidis</i> , <i>Bacillus enteritidis sporogenes</i> , <i>Bacillus sporogenes</i> Variants: <i>Clostridium sporogenes</i> var. A. P. MARIE PRÉVOT <i>Clostridium sporogenes</i> var. <i>equine</i> PRÉVOT <i>Clostridium flabilliferum</i> STURGES et REDDISH <i>Clostridium parasporogenes</i> (BULLOCH et al.) BERGEY et al.	+	anaerobe, gas-former	Regularly in manured soils, intestinal tract	All variants are patho-gens of gas gangrene.	1	0	2	

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name Synonyms	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. application of antibiotics			Remarks
			Gram's staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) - continued								
72	116	Clostridium bifermentans (WEINBERG et SEGUIN) BERGEY et al. <i>Bacillus bifermentans sporogenes</i> , <i>Bacillus sporogenes oedematis</i> , <i>Clostridium centrosporogenes</i> , <i>Clostridium foetidum</i> , <i>Clostridium oedematoides</i> , <i>Clostridium sordelli</i> , <i>Clostridium sporogenes</i> var. B, <i>Martellillus bifermentans</i>	+	anaerobe, gas-former	Faeces, soil and sewage	Pathogen of gas gangrene, produces a violent toxin.	1	0	2	Plus antitoxin.
72	117	Clostridium perfringens (VEILLON et ZUBER) HOLLAND <i>Bacillus aerogenes capsulatus</i> , <i>Bacillus amylobacter immobilis</i> , <i>Bacillus butyricus asporogenes immobilis</i> , <i>Bacillus capsulatus aerogenes</i> , <i>Bacillus emphysematis vaginae</i> , <i>Bacillus emphysematosus</i> , <i>Bacillus phlegmones emphysematosae</i> , <i>Bacillus welchii</i> , <i>Bacterium aerogenes capsulatus</i> , <i>Bacterium emphysematosus</i> , <i>Bacterium welchii</i> , <i>Butyribacillus immobilis-liquefaciens</i> , <i>Cillobacterium multiforme</i> , <i>Clostridium aerogenes-capsulatum</i> , <i>Clostridium phlegmones emphysematosae</i> , <i>Clostridium welchii</i> , <i>Welchia perfringens</i> , <i>Welchillus aerogenes</i>	+	anaerobe, gas-former	Faeces, soil and sewage	Pathogen of gas gangrene, produces a violent toxin.	1	0	2	Plus antitoxin.
72	118	Clostridium sphenoides (BULLOCH et al.) BERGEY et al. <i>Douglasillus sphenoides</i> , <i>Plectridium sphenoides</i>	only in young cultures +	anaerobe, gas-former		Pathogen of gas gangrene.	1	0	2	
72	119	Clostridium innominatum PRÉVOT <i>Bacillus</i> E ADAMSON	-	anaerobe		Isolated from septic and gangrenous war wounds.	1	0	2	
72	120	Clostridium paraputrificum (BIENSTOCK) SNYDER <i>Acuformis innutritus</i> , <i>Bacillus diaphthirus</i> , <i>Bacillus paraputrificus</i> , <i>Bacillus paraputrificus coli</i> , <i>Plectridium paraputrificum</i> , <i>Tissierellus paraputrificus</i>	+	anaerobe, gas-former	Regularly in intestinal tract	Pathogen of gas gangrene.	1	0	2	
72	121	Clostridium capitoale (SNYDER et HALL) SNYDER <i>Bacillus capitoalis</i> , <i>Plectridium capitoalis</i>	+	anaerobe, gas-former	Intestinal tract	Pathogen of gas gangrene.	1	0	2	
72	122	Clostridium tetanoides (ADAMSON) HAUDUROY et al. <i>Acuformis macrosporus</i> , <i>Bacillus tetanoides</i> , <i>Palmula macrospora</i>	-	anaerobe	Soil	Pathogenicity uncertain, isolated from war wounds.	1	0	2	
72	123	Clostridium tetani (FLÜGGE) HOLLAND <i>Bacillus tetani</i> , <i>Nicollaierillus tetani</i> , <i>Pacinia tetani</i> , <i>Flectridium tetani</i> , tetanus bacillus	+	anaerobe	Soil, intestinal tract	Pathogen of tetanus, produces a violent neurotoxin.	Antitoxin 1	0	2	Active tetanus vaccination usually confers lifelong immunity. Every child should be vaccinated at an early age (6-8 months), with a repeat injection several years later.
72	124	Clostridium lentoputrescens HARTSELL et RETTGER <i>Bacillus albuminis</i> , <i>Bacillus butyricus putrefaciens</i> , <i>Bacillus putrificus coli</i> , BIENSTOCK's bacillus, <i>Clostridium putrificum</i> , <i>Pacinia putrifica</i> , <i>Plectridium putrificum</i> , <i>Putribacillus vulgaris</i>	-	anaerobe	Soil, intestinal tract	Usually non-pathogenic.	1	0	2	

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. application of antibiotics			Remarks
			Gram's staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) - continued								
72	125	Clostridium alcaligenes BERGEY et al. <i>Acuformis alcaligenes, Bacillus anaerobicus alcaligenes, Palmula alcaligenes</i>	+	anaerobe	Intestinal tract	Usually non-pathogenic.	1	0	2	
72	126	Clostridium histolyticum (WEINBERG et SEGUIN) BERGEY et al. <i>Bacillus histolyticus, Weinbergillus histolyticus</i>	+	anaerobe to micro-aerophil		Isolated from war wounds, causes necrosis.	1	0	2	
72	127	Clostridium tertium (HENRY) BERGEY et al. <i>Bacillus tertius, Henrillus tertius, Palmula spermoides, Plectridium gazogenes</i>	+	anaerobe and micro-aerophil	Widely distributed in soil, in sewage, intestinal tract	Isolated from gangrenous wounds, produces a violent toxin.	1	0	2	Plus antitoxin.
101	128	Mycobacterium tuberculosis var. hominis and var. bovis * (SCHROETER) LEHMANN et NEUMANN <i>Bacillus tuberculosis, Bacterium tuberculosis, Coccothrix tuberculosis, Discomyces tuberculosis, Eumyces tuberculosis, Sclerothrix kochii, Sclerothrix tuberculosis</i>	+	?	<i>M. t. var. bovis</i> : in affected cows and man; <i>M. t. var. hominis</i> : in man	<i>M. tuberculosis</i> var. <i>bovis</i> : pathogen of bovine tuberculosis, pathogenic also for man (ca. 10% of all cases of tuberculosis, varying from country to country); <i>M. t. var. hominis</i> : pathogen of human tuberculosis, for animals less pathogenic than var. <i>bovis</i> .	see footnote			See footnote*.
101	129	Mycobacterium leprae (ARMAUER-HANSEN) LEHMANN et NEUMANN <i>Coccothrix leprae, Discomyces leprae, Sclerothrix leprae</i>	+	?	In patients only	Pathogen of leprosy, possesses a marked affinity for the skin and peripheral nerves. Does not affect the internal organs. -Experimental transmission to man or animals has not yet been achieved.	0	0	0	Sulphones (glucosulphone sodium, sulphoxone sodium, etc.), thi-acetazone. Cf. ¹ .

* Tuberculosis and antibiotics

A critical appreciation of the mass of literature on this subject would hardly be of great value to the practitioner, quite apart from its being almost an impossibility in view of the great variety of methods of treatment, healing criteria, etc. which have been employed in the various investigations. For this reason it has been decided to base this short summary on the results of a single research group (Veterans Administration, USA), which since 1946 has carried out an unbroken series of investigations based on uniform criteria and involving the collaboration of 50 hospitals (to date 15,000 individual treatments)². Unless otherwise stated the following text refers to pulmonary tuberculosis.

The toxicity of streptomycin and the rapidly increasing resistance of the tubercle bacilli set a limit for some years to the scope and duration of antibiotic treatment in tuberculosis. The principal indications in which an unquestionable success was achieved were in the acute stages such as miliary tuberculosis, tubercular meningitis, and in the preoperative field. In chronic cases an initial healing was always overtaken by the increase in resistance. The duration of treatment was limited to 3-4 months at the most.

With the appearance of further tuberculostatics, first of all *p*-aminosalicylic acid (PAS), followed by isoniazid and related compounds, terramycin (oxytetracyclin), viomycin and the thio-

semicarbazones, the situation changed. It became possible to use antibiotic combinations which permitted on the one hand the dosage and thus the toxicity of particular components to be reduced, and on the other hand the increase of resistance to be delayed considerably or, by appropriate changes in components or combinations, to be overcome. There was no further hindrance to extending the duration of treatment and the number of successful treatments of average cases of pulmonary tuberculosis was markedly increased. It should be noted, however, that the figures for successful treatments here included cases where other therapeutic methods had been applied, such as hospitalization, pneumothorax, surgery, etc. To what extent future indication of these methods will be affected by antibiotic treatment remains to be seen. There is already, however, an unmistakable tendency to a more cautious approach. For example, the results of antibiotic treatment are first awaited before surgery is resorted to.

Experience has now shown that treatment should extend without interruption over 12 months or more. Breaks in treatment should be avoided. In 60-80% of (not pre-treated) cases a bacteria-free sputum has been thereby achieved, and in 80% of cases a significant improvement in the radiograph. Cavities up to 6 cm diameter have closed without pneumothorax. Cavities remaining open after 6 months should be treated surgically: in such cases a sputum test which has become negative usually reverts

(continued on next page)

¹) DAVIDSON, W. S., *Leprosy Rev.*, **24**, 139, 1953. ²) D'ESORO, N., Report to the Council (Council on Pharmacy and Chemistry): Chemotherapy of Tuberculosis in Man, Present Status, *J. Amer. med. Ass.*, **154**, 52, 1954.

See pages 169-171	See pages 172-178	Name Synonyms	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. appli- cation of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
102	130	Bacteria (Schizomycetes) - continued Nocardia asteroides (EPPINGER) BLANCHARD <i>Actinomyces asteroides, Actinomyces eppingeri, Asteroides asteroides, Cladothrix asteroides, Discomyces asteroides, Oospora asteroides, Proactinomyces asteroides, Streptothrix asteroides</i>	acido-phil	aerobe		Actinomycosis.	1	?	2	Plus sulphonamides.
102	131	Nocardia leishmanii CHALMERS et CHRISTOPHERSON <i>Actinomyces leishmani, Discomyces leishmani</i>	acido-phil	aerobe		Actinomycosis.	1	?	2	Plus sulphonamides.
102	132	Nocardia madurae (VINCENT) BLANCHARD <i>Actinomyces indicus, Actinomyces madurae, Cladothrix madurae, Discomyces indicus, Discomyces madurae, Oospora indica, Oospora madurae, Streptothrix madurae</i>	non-acido-phil	aerobe		Associated with maduramycosis (Madura foot) but not always the direct cause of this disease.	1	?	2	
102	133	Nocardia lutea CHRISTOPHERSON et ARCHIBALD <i>Actinomyces luteus</i>		aerobe		Actinomycosis.	1	?	2	
103	134	Actinomyces bovis HARZ <i>Actinomyces bovis sulphureus, Actinomyces sulphureus, Cladothrix actinomyces, Cladothrix bovis, Discomyces bovis, Nocardia actinomyces, Nocardia bovis, Nocardia sulphurea, Proactinomyces bovis, Sphaerotilus bovis, Streptothrix actinomycotica, Streptothrix bovis, Streptothrix bovis communis</i>	non-acido-phil	anaerobe to micro-aerophil		Cause of actinomycosis in cattle, sometimes also in man.	1	?	2	

to positive since the tubercle bacilli in the cavities remain virulent in spite of antibiotic treatment. This is particularly stressed because tubercle bacilli from caseous, capsulated foci are only 5-10% virulent (virulence tested on animals). There are still differences of opinion whether such residual foci should be surgically removed. In view of the particularity mentioned, the tendency is to eliminate the larger ones and leave the others.

The above therapeutic results are based on a combination therapy which has been systematically applied over a long period, i.e. streptomycin 1 g (15 grains) twice weekly plus PAS 12 g (185 grains) daily. This dosage is sufficient in most cases. In those cases where the resistance to PAS nevertheless increases, the streptomycin dose should be increased to 1 g (15 grains) daily. In view of the danger of possible permanent lesions streptomycin is unquestionably to be preferred to dihydrostreptomycin. It is not yet possible to say whether the recently proposed 50:50 mixture of these two compounds¹ will prove in the long run to be less toxic than streptomycin alone.

The combination streptomycin 1 g twice weekly plus isoniazid 0.3 g (5 grains) daily is apparently equally efficacious, although it should be noted that its apparent superiority over streptomycin + PAS at the beginning of therapy is due only to the marked euphoric effect of isoniazid. In any case the results observed to date are insufficient to show which of these methods will eventually prove superior.

Terramycin (oxytetracyclin) alone is valueless as a tuberculostatic but in combination (1-2 g [15-30 grains] daily + 1 g [15 grains] streptomycin twice weekly) it is effective and of particular value where a resistance to PAS or isoniazid has developed.

Viomycin and the thiosemicarbazones are too toxic and not effective enough to be considered as important tuberculostatics. They are useful in cases where a resistance to one of the previously mentioned agents has developed, or for special cases. Thus the thiosemicarbazones have proved to be greatly superior to other agents in several cases of tuberculosis of the mucosa (tuberculous laryngitis, intestinal tuberculosis).

Present experience with the antibiotics and chemotherapeutics available for combating tuberculosis may be summarized as follows: in the front rank stands streptomycin, in the second PAS and isoniazid, with terramycin, viomycin and the thiosemicarbazones some distance behind. Tubercle bacilli rapidly develop resistance to all agents administered alone, whereas this is much less marked when combinations are administered. Of the combinations only streptomycin + PAS has been shown by extensive and lengthy investigations to be more or less of confirmed therapeutic value. The combination streptomycin + isoniazid appears to be equally effective, while all other combinations must still be considered as experimental.

¹) Editorial, *Medicus*, 5, 207, 1953.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name Synonyms	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. application of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) - continued								
103	135	Actinomyces israeli (KRUSE) LACHNER-SANDOVAL <i>Actinobacterium israeli</i> , <i>Actinomyces wolff-israeli</i> , <i>Actinomyces israeli</i> , <i>Anaeromyces bronchitica</i> , <i>Brevistreptothrix israeli</i> , <i>Cohnistreptothrix bronchitica</i> , <i>Cohnistreptothrix israeli</i> , <i>Corynebacterium israeli</i> , <i>Discomyces israeli</i> , <i>Nocardia israeli</i> , <i>Oospora israeli</i> , <i>Proactinomyces israeli</i> , <i>Streptothrix israeli</i>	non-acidophil	anaerobe to micro-aerophil		Actinomycosis (man and animals).	1	?	2	
104	136	Streptomyces fordii comb. nov. (ERIKSON) <i>Actinomyces fordii</i>		aerobe		Actinomycosis.	1	?	2	
104	137	Streptomyces africanus comb. nov. (PIJPER et PULLINGER) <i>Actinomyces africanus</i>		aerobe		Actinomycosis.	1	?	?	
104	138	Streptomyces gallicus comb. nov. (ERIKSON) <i>Actinomyces gallicus</i>		aerobe		Actinomycosis.	1	?	?	
104	139	Streptomyces pelletieri comb. nov. (LAVERAN) <i>Actinomyces pelletieri</i> , <i>Discomyces pelletieri</i> , <i>Micrococcus pelletieri</i> , <i>Nocardia pelletieri</i> , <i>Oospora pelletieri</i>		aerobe		Actinomycosis.	1	?	?	
104	140	Streptomyces listeri comb. nov. (ERIKSON) <i>Actinomyces listeri</i>		aerobe		Actinomycosis.	1	?	?	
104	141	Streptomyces upcottii comb. nov. (ERIKSON) <i>Actinomyces upcottii</i>		aerobe		Actinomycosis.	1	?	?	
104	142	Streptomyces hortonensis comb. nov. (ERIKSON) <i>Actinomyces hortonensis</i>		aerobe		Actinomycosis.	1	?	?	
104	143	Streptomyces gibsonii comb. nov. (ERIKSON) <i>Actinomyces gibsonii</i>		aerobe		Actinomycosis.	1	?	?	
104	144	Streptomyces beddardii comb. nov. (ERIKSON) <i>Actinomyces beddardii</i>		aerobe		Actinomycosis.	1	?	?	
104	145	Streptomyces kimberi comb. nov. (ERIKSON) <i>Actinomyces kimberi</i>		aerobe		Actinomycosis.	1	?	?	
104	146	Streptomyces somaliensis comb. nov. (BRUMPT) <i>Actinomyces somaliensis</i> , <i>Discomyces somaliensis</i> , <i>Indiella somaliensis</i> , <i>Indiellopsis somaliensis</i> , <i>Nocardia somaliensis</i> , <i>Streptothrix somaliensis</i>		aerobe		Actinomycosis.	1	?	?	

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. application of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
104	147	Bacteria (Schizomycetes) – continued <i>Streptomyces willmorei</i> comb. nov. (ERIKSON) <i>Actinomyces willmorei</i>		aerobe		Actinomycosis.	1	?	?	
137	148	<i>Borrelia recurrentis</i> (LEBERT) BERGEY et al. <i>Cacospira obermeieri</i> , <i>Cacospira recurrentis</i> , <i>Protomycetum recurrentis</i> , <i>Spirillum obermeieri</i> , <i>Spirillum recurrentis</i> , <i>Spirochaeta obermeieri</i> , <i>Spirochaeta recurrentis</i> , <i>Spironema obermeieri</i> , <i>Spironema recurrentis</i> , <i>Spiroschaudinnia obermeieri</i> , <i>Spiroschaudinnia recurrentis</i> , <i>Treponema obermeieri</i> , <i>Treponema recurrentis</i>	–		Transmitted by the body louse (<i>Pediculus humanus</i>)	European relapsing fever.	1	0	2	
137	149	<i>Borrelia duttonii</i> (BREINL) BERGEY et al. <i>Cacospira duttoni</i> , <i>Spirillum duttoni</i> , <i>Spirochaeta duttoni</i> , <i>Spironema duttoni</i> , <i>Spiroschaudinnia duttoni</i> , <i>Treponema duttoni</i>	–		Transmitted by ticks (<i>Ornithodoros moubata</i>)	Relapsing fever of Central and South Africa, tick fever.	1	0	2	
137	150	<i>Borrelia kochii</i> (NOVY) BERGEY et al. <i>Borrelia rossi</i> , <i>Spirochaeta kochi</i> , <i>Spirochaeta rossi</i> , <i>Spironema kochii</i> , <i>Spiroschaudinnia rossi</i> , <i>Treponema kochi</i> , <i>Treponema rossi</i>			Vector?	African relapsing fever.	1	0	2	
137	151	<i>Borrelia novyi</i> (SCHELLACK) BERGEY et al. <i>Cacospira novyi</i> , <i>Spirochaeta novyi</i> , <i>Spironema novyi</i> , <i>Spiroschaudinnia novyi</i> , <i>Treponema novyi</i>			Vector?	American relapsing fever.	1	0	2	
137	152	<i>Borrelia carteri</i> (MACKIE) BERGEY et al. <i>Spirillum carteri</i> , <i>Spirochaeta carteri</i> , <i>Spironema carteri</i> , <i>Spiroschaudinnia carteri</i> , <i>Treponema carteri</i>			Vectors: lice (<i>Pediculus humanus</i>) and bedbugs (<i>Cimex rotundatus</i>)	Indian relapsing fever.	1	0	2	
137	153	<i>Borrelia vincentii</i> (BLANCHARD) BERGEY et al. <i>Spirochaeta plaut-vincenti</i> , <i>Spirochaeta schaudinni</i> , <i>Spirochaeta vincenti</i> , <i>Spironema vincenti</i> , <i>Spiroschaudinnia schaudinni</i> , <i>Spiroschaudinnia vincenti</i> , <i>Treponema schaudinni</i> , <i>Treponema vincenti</i>	–		Mucosa of the respiratory passages	Cause of PLAUT-VINCENT angina, together with <i>Fusobacterium plauti-vincenti</i> (94).	1	0	2	
137	154	<i>Borrelia refringens</i> (SCHAUDINN et HOFFMANN) BERGEY et al. <i>Spirochaeta refringens</i> , <i>Spironema refringens</i> , <i>Spiroschaudinnia refringens</i> , <i>Treponema refringens</i>			Genital mucosa	Non-pathogenic.	1	0	2	
137	155	<i>Borrelia hermsi</i> (DAVIS) STEINHAUS <i>Spirochaeta hermsi</i>			Vector: ticks (<i>Ornithodoros hermsi</i>)	Relapsing fever of western North America.	1	0	2	
137	156	<i>Borrelia parkeri</i> (DAVIS) STEINHAUS <i>Spirochaeta parkeri</i>			Vector: ticks (<i>Ornithodoros parkeri</i>)	Relapsing fever of western North America.	1	0	2	
137	157	<i>Borrelia turicatae</i> (BRUMPT) STEINHAUS <i>Spirochaeta turicatae</i>			Vector: ticks (<i>Ornithodoros turicata</i>)	Relapsing fever in Mexico, Texas and neighbouring areas.	1	0	2	

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. appli- cation of antibiotics			Remarks
		Name	GRAM'S staining			Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) - continued							
137	158	Borrelia venezuelensis BRUMPT <i>Treponema venezuelensis</i>		Vector: ticks (<i>Ornithodoros rudis</i> or <i>venezuelensis</i>)	Relapsing fever in Pan- ama.	1	0	2	
138	159	Treponema pallidum* (SCHAUDINN et HOFFMANN) SCHAUDINN <i>Microspironema pallidum</i> , <i>Spirochaeta pallida</i> , <i>Spironema pallidum</i> , <i>Trypanosoma luis</i>	anaerobe	Transmitted by bodily contact	Syphilis.	1	0	2	See footnote*.
138	160	Treponema pertenue CASTELLANI <i>Spirochaeta pallidula</i> , <i>Spirochaeta pertenuis</i> , <i>Spironema pertenue</i> , <i>Treponema pallidulum</i> , <i>Tréponème du pian</i>	anaerobe		Yaws. Synonyms: fram- besia, pian, patek (Ma- laya), parangi (Ceylon), for others see remarks.	2	0	1	Other synonyms for yaws: tonga (New Caledonia), coco (Fiji Islands), aboukoué or ab-oukine (Gabun).
138	161	Treponema mucosum NOGUCHI <i>Spirochaeta mucosa</i>	obligate anaerobe		Isolated from alveolar pus. Possesses pyogen- ic properties.	1	0	2	
138	162	Treponema calligyrum NOGUCHI <i>Spirochaeta calligyra</i>	anaerobe	Genitals	Non-pathogenic.	1	0	2	
138	163	Treponema genitalis NOGUCHI <i>Spirochaeta genitalis</i> , <i>Treponema minutum</i>	anaerobe	Genitals	Non-pathogenic.	1	0	2	

* Syphilis and antibiotics¹⁻⁸ et al.

Since the first application of penicillin to syphilis by ARNOLD and MAHONEY in 1943⁶ a revolution in the treatment of this disease has taken place. Penicillin has proved markedly superior to arsenic and bismuth preparations and there exists no further reason for using the latter except perhaps in very special cases⁷. Development of resistance to penicillin by the pathogen of syphilis has as yet been nowhere reported. It is as effective in the treatment of relapses⁸ as in initial treatment.

The main advantages of penicillin therapy consist in the rapid disappearance of the infectiousness (1-2 days after the first injection), the low toxicity, the much rarer and feebler HERXHEIMER reactions, and not least in the short duration of treatment (2-3 weeks). This is valid for all stages and forms of syphilis. Even those cases which earlier resisted all chemotherapeutic treatments, such as certain neurolytic, tabetic and paralytic forms, react promptly to penicillin. It cannot of course heal anatomical lesions which already exist.

As a matter of routine the dosage should be high, between 5 and 20 million units in a period of 2-3 weeks, the lower figure for early stages and the higher for the later stages of the disease. Patients who for any reason cannot be hospitalized should be given an injection of 2-3 million units depot-penicillin at the first consultation in order to ensure that they cease for a considerable time to be a source of infection for their environment.

After treatment all patients should be retained for as long as

possible under clinical and serological control so that any eventual failure or relapse may be immediately detected. Here it should be noted that the serological improvement proceeds only slowly and lags some months behind the clinical improvement, especially in all late forms of syphilis. Older patients often continue indefinitely to show a positive WASSERMANN reaction and in cases showing clear clinical improvement this should not be taken as evidence of a persistent morbid process.

Adequate penicillin treatment of a syphilitic mother during pregnancy will result in a 95% chance of the child being healthy. Since the WASSERMANN antibodies pass the placental barrier, a positive WASSERMANN reaction of the cord blood is no indication, in the absence of other clinical symptoms, that immediate treatment of the child is necessary. The latter is only necessary when after several months the antibody titre remains at a high level or has risen.

Of the remaining antibiotics the tetracyclins appear to be as effective as penicillin, although sufficient observations for a reliable comparison have not as yet been made. In any case penicillin is likely on purely economic grounds to retain for some time its position as the leading antisypilitic. The use of the tetracyclins would on the other hand be justified in the case of patients who cannot tolerate penicillin and they are the antibiotics of choice for the treatment of the closely related disease of yaws (the possibility of oral administration is a great advantage in medically backward countries).

¹) Symposium on Syphilis, *Amer. J. Med.*, **5**, 629, 1948. ²) ALEXANDER et al., *Arch. Derm. Syph. (Chicago)*, **33**, 1, 1949; *ibid.*, **34**, 420, 1950. ³) WALKER and STOUGHTON, *Med. Clin. N. Amer.*, **35**, 143, 1951. ⁴) MIESCHER and BRENN, *Schweiz. med. Wschr.*, **82**, 917, 1952. ⁵) FLOREY, M. F., *The Clinical Application of Antibiotics* (Penicillin), Oxford University Press, 1952. ⁶) ARNOLD and MAHONEY, *J. vener. Dis. Inform.*, **24**, 355, 1943. ⁷) For pre-treatment of severe cases of cardiovascular syphilis: bismuth sodium tartrate 1 ml of a 1.5% solution three times weekly for 3-5 weeks; no arsenic preparations. ⁸) Ca. 10-20%. The question of "relapses" should be treated with care. It is frequently a case of reinfection, which is indistinguishable from a relapse.

See pages 169-171	See pages 172-178	Name Synonyms	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. application of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
138	164	Bacteria (Schizomycetes) – continued Treptonema carateum BRUMPT <i>Treponema herrejoni</i> , <i>Treponema pictor</i> , <i>Treponema pintae</i>		anaerobe		Pinta. Synonyms: pinto, mal de los pintos, carate, azul, boussarole, spotted sickness.	1	0	2	WASSERMANN, KAHN, and MEINICKE tests positive.
139	165	Leptospira icterohaemorrhagiae* (INADA et IDO) NOGUCHI <i>Leptospira icterogenes</i> , <i>Leptospira nodosa</i> , <i>Spirochaeta icterohaemorrhagiae</i> , <i>Spirochaeta nodosa</i> , <i>Spiroschaudinna icterohaemorrhagiae</i> , <i>Treponema icterogenes</i> , <i>Treponema nodosum</i>		aerobe	Water and mud; host: <i>Rattus norvegicus</i>	Leptospiral jaundice. Synonyms: WEIL's disease, infectious spirochaetal jaundice, FIEDLER's disease.	1	0	2	See footnote*.

* Leptospirosis¹⁻⁴

In *Bergey's Manual*⁵, on which the systematic classification given in these tables is based, the *Leptospira* (165-167) are shown as species. According to BROOM¹ and GSELL² they are better classified according to their antigenic properties as "serotypes" pending a final definition of their taxonomic status. Up to now 40 different serological types have been distinguished, of which the most important are:

Serotype	Principal host	Disease	Distribution
<i>L. australis A</i>	<i>Rattus culmorum</i>	Cane-sugar fever, field fever	Very widely distributed
<i>L. australis B</i>	<i>Rattus connatus</i>	Short-lived leptospiral fever	Australia
<i>L. autumnalis</i>	<i>Apodemus speciosus</i> , <i>Microtus montebelloi</i> , <i>Rattus brevicaudatus</i>	Japanese autumn fever (aki-yami), Fort Bragg fever, tibial fever (USA)	Japan, south-east Asia, USA
<i>L. bovis</i>	<i>M. güntheri</i> (?) Cattle	Icterohaemoglobinuria of cattle	Europe, Israel, Asia
<i>L. canicola</i>	Dog	Canicola fever	Very widely distributed
<i>L. grippotyphosa</i>	<i>Microtus arvalis</i> <i>Microtus agrestis</i> <i>Apodemus sylvaticus</i> <i>Evotymis glareolus</i>	Swamp fever, mud fever, marsh fever, water fever, harvest fever, pea-pickers' disease, Charente fever	Europe, Israel, Asia
<i>L. hebdomadis</i>	<i>Microtus montebelloi</i>	Japanese seven-day fever (nanuka-yami, giki-yami)	Japan, south-east Asia
<i>L. icterohaemorrhagiae</i>	<i>Rattus norvegicus</i>	Leptospiral jaundice	Very widely distributed
<i>L. mitis</i>	Pig	Swineherd's disease	Very widely distributed
<i>L. pomona</i>	Pig	As for <i>L. mitis</i>	Very widely distributed
<i>L. pyrogenes</i>	<i>Rattus brevicaudatus</i>	Short-lived leptospiral fever	South-east Asia, Australia

Clinical treatment of leptospirosis

The incubation period lasts as a rule about 10 days, with variations from 3 to 20 days. Children are very seldom affected, and icteric forms of the disease are usually observed only at the age of 30 years on. Commencement is acute and premonitory symptoms rare. The fever often begins with bouts of shivering and usually has a diphasic course. The patient complains of severe headache, photophobia, muscular pains in the back and limbs (especially the

calves). Vomiting and abdominal pains indicate an acute affection of the abdomen. Congestion of the conjunctival vessels of varying duration is often, but not always, observed. Depression is very marked, the patient looking and feeling worse than the objective symptoms would indicate.

Severe, icteric form (15-30% mortality). Typical for leptospiral jaundice. Characterized by rapidly rising fever up to 102°F (39°C) and higher, lasting about 1 week, followed by lytic fall. Icterus commences on the 5th day and reaches a maximum on the 8th or 9th day. At this point haemorrhages in the form of epistaxis, melaena, haematuria, cutaneous and mucous haemorrhages, usually occur. Blood pressure is often alarmingly low. Leucocytosis (15,000 to 25,000) occurs, in contrast to the benign form, also nephritis, oliguria, in fatal cases anuria with death in a uraemic coma. In the case of recovery the condition of the patient improves with the first attack of fever, which is usually followed by a second, weaker attack. Convalescence is slow.

Benign, non-icteric form. This occurs in two forms. The first, typical for Japanese autumn and seven-day fever (*L. autumnalis*, *L. hebdomadis*) differs only in the severity of the symptoms from the icteric form. The second variety, typical for swineherd's disease (*L. pomona*, *L. mitis*) and swamp fever (*L. grippotyphosa*), is characterized by predominating meningeal symptoms: severe headache, often combined with vertigo, loss of consciousness, nuchal rigidity and positive KERNIG (differential diagnosis of lymphocytic choriomeningitis). Muscular weakness and paresis can give the appearance of poliomyelitis. The eyes are usually also affected: nystagmus, diplopia, iritis, pupillary irregularities. Short-lived exanthema in various forms is often observed; profuse sweating is a frequent early symptom. Cell and protein contents of the cerebrospinal fluid are increased, sugar content is normal. In contrast to the severe form leucocytes are usually normal. Nephritic symptoms and albuminuria are observed, according to the severity of the case. Defervescence proceeds as in the severe form, convalescence is slow.

Diagnosis: anamnesis (professional activity), symptoms. Confirmation of the diagnosis by identification of the pathogen or after the second week by serological detection of antibodies.

Therapy: There is general agreement that antibiotic treatment has no influence on the course of the disease if commenced 8 days after the first appearance of symptoms. Penicillin has practically no effect. Most efficacious are the tetracyclins. – An appropriate non-specific therapy, with particular emphasis on renal function and electrolyte metabolism, is of primary importance.

1) BROOM, J. C., *Trans. roy. Soc. trop. Med. Hyg.*, **47**, 273, 1953. 2) GSELL, O., *Leptospirosen*, Berne, 1952. 3) BEESON, P. B., *Amer. J. Med.*, **15**, 591, 1953. 4) HALL et al., *Ann. intern. Med.*, **35**, 981, 1951. 5) BREED et al., *Bergey's Manual of Determinative Bacteriology*, New York, 1948.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. application of antibiotics			Remarks
			GRAM's staining				Penicillin	Streptomycin	Tetracyclins	
		Bacteria (Schizomycetes) - continued								
139	166	Leptospira hebdomadis (IDO et al.) NOGUCHI <i>Spirochaeta hebdomadis</i> , <i>Spirochaeta nanukayami</i> , <i>Spiroschaudinnia hebdomadis</i> , <i>Treponema hebdomadis</i>		aerobe	Host: field vole (<i>Microtus montibelloi</i>)	Japanese seven-day fever (nanuka-yami, giki-yami).	0	0	1	See footnote* on previous page.
139	167	Leptospira canicola OKELL et al.		aerobe	Dogs	In older dogs, chronic illness with uraemia (no icterus). Occasionally also in man (canicola fever).	0	0	1	See footnote* on previous page.
140	168	Rickettsia prowazekii DA ROCHA-LIMA <i>Rickettsia exanthematotypbi</i>	-		Transmitted by lice: <i>Pediculus humanus</i> var. <i>corporis</i> and var. <i>capitis</i> , <i>Pediculus longiceps</i>	Classical typhus fever (European, epidemic), BRILL's disease (after BRUMPT), exanthematous typhus.	0	0	1	Antibiotics of choice: tetracyclins.
140	169	Rickettsia typhi (WOLBACH et TODD) PHILIP <i>Dermacentroxenus typhi</i> , <i>Rickettsia exanthematofebri</i> , <i>Rickettsia fletcheri</i> , <i>Rickettsia manchuriae</i> , <i>Rickettsia mooseri</i> , <i>Rickettsia muricola</i> , <i>Rickettsia murina</i>	-		Transmitted by fleas: <i>Xenopsylla cheopis</i> , <i>Xenopsylla astia</i> , <i>Echidnophaga gallinacea</i> , <i>Polyplax spinulosus</i>	Endemic (murine) typhus (benign typhus), tabardillo (Latin America).	0	0	1	As above (168).
140	170	Rickettsia rickettsii (WOLLBACH) BRUMPT <i>Dermacentroxenus rickettsii</i> var. <i>brasiliensis</i> , <i>Rickettsia brasiliensis</i> , <i>Rickettsia dermacentroxenus</i>	-		Transmitted by ticks: <i>Dermacentor andersoni</i> , <i>Dermacentor variabilis</i> , <i>Haemaphysalis leporis-palustris</i> , <i>Amblyomma brasiliensis</i> , <i>Amblyomma cajennense</i> , <i>Amblyomma striatum</i> , <i>Amblyomma americanum</i> , <i>Ixodes dentatus</i>	Rocky Mountain spotted fever, São Paulo typhus, Tobia fever (Columbia), Minas-Gerais typhus (Brazilian macular fever).	0	0	1	As above (168). Cf. ¹ .
140	171	Rickettsia conorii BRUMPT <i>Dermacentroxenus conorii</i> , <i>Dermacentroxenus rickettsii</i> var. <i>conorii</i> , <i>Dermacentroxenus rickettsii</i> var. <i>pijperi</i> , <i>Rickettsia blanci</i> , <i>Rickettsia megawi</i>	-		Transmitted by ticks: <i>Rhipicephalus sanguineus</i> , <i>Amblyomma hebraeum</i> , <i>Haemaphysalis leachi</i> , <i>Rhipicephalus appendiculatus</i> , <i>Boophilus decoloratus</i>	Boutonneuse fever, Mediterranean exanthematous fever, eruptive Mediterranean fever, OLMER's disease.	0	0	1	As above (168). Cf. ² .
140	172	Rickettsia tsutsugamushi (HAYASHI) OGATA <i>Dermacentroxenus orientalis</i> , <i>Rickettsia akamushi</i> , <i>Rickettsia megawi</i> var. <i>fletcheri</i> , <i>Rickettsia orientalis</i> , <i>Rickettsia pseudotypbi</i> , <i>Rickettsia tsutsugamushi-orientalis</i> , <i>Tbeileria tsutsugamushi</i>	-		Transmitted by mites: <i>Trombicula akamushi</i> , <i>Trombicula deliensis</i> , <i>Trombicula fletcheri</i>	Tsutsugamushi disease, scrub typhus, Japanese river fever, flood fever, Kedani fever, Shimamushi mite-borne typhus, Delhi pseudo-typhus.	0	0	1	As above (168).
140	173	Rickettsia quintana SCHMINKE <i>Fossilis quintana</i> , <i>Rickettsia wolbynica</i>	-		Transmitted by lice: <i>Pediculus humanus</i> var. <i>corporis</i> and var. <i>capitis</i>	Five-day fever, trench fever, quintan fever, Volhynia fever, tibial-gic fever.	0	0	1	As above (168).

¹) BAKER, E. G., *Med. Clin. N. Amer.*, **35**, 907, 1951. ²) GAC and ROOBY, *Bull. Soc. Path. exot.*, **43**, 678, 1950.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics		Habitat, host, transmission, etc.	Diseases	Clin. application of antibiotics			Remarks
			Gram's staining				Penicillin	Streptomycin	Tetracyclins	
141	174	Bacteria (Schizomycetes) - continued Coxiella burnetii comb. nov. (DERRIK) BENGTON	-		Transmitted by ticks: <i>Dermacentor andersoni</i> , <i>Dermacentor occidentalis</i> , <i>Amblyomma americanum</i> , <i>Haemaphysalis leporis-palustris</i> , <i>Haemaphysalis humerosa</i>	Q fever, Queensland fever, quadrilateral fever.	0	0	1	Antibiotics of choice : tetracyclins. Now distributed over the whole world, including Europe. Here it is very probably dust- or milk-borne. For a brief review, see ¹ .
143	175	Bartonella bacilliformis (STRONG et al.) STRONG et al. <i>Bartonella coccoide</i> , <i>Bartonella peruviana</i> , <i>Bartonia bacilliformis</i> , <i>Eperthyrozoön noguchii</i>	-	obligate aerobe	Transmitted by sand flies: <i>Phlebotomus verrucarum</i> , <i>Phlebotomus noguchii</i>	CARRION's disease, Or- oya fever, verrugaperu- ana.	0	0	1	See above (174).
147	176	Chlamydozoon trachomatis FOLEY et PARROT <i>Rickettsia trachomae</i> , <i>Rickettsia trachomatis</i>	-			Trachoma.	2	?	1	See above (174). For a brief review, see ² .
147	177	Chlamydozoon oculo- genitale MOSHKOVSKY	-		Contaminated water	Inclusion conjunctivitis (inclusion blennor- rhoea, infantile conjunc- tivitis), swimming pool conjunctivitis.	0	0	1	See above (174). For a brief review, see ² .
148	178	Miyagawanella lympho- granulomatis BRUMPT <i>Ehrlichia lymphogranulomatosi</i> , <i>Virus lympho-granulomateux</i>	-		Transmitted by venereal contact	Venereal lymphogranu- loma, lymphogranulo- ma inguinale, climatic bubo, esthiomene, NI- COLAS-FAVRE disease.	0	0	1	See above (174). World- wide distribution. For a brief review, see ² .
148	179	Miyagawanella psittaci (LILLIE) MOSHKOVSKY <i>Ehrlichia psittaci</i> , <i>Microbacte- rium multiforme psittacosis</i> , parrot virus, <i>Rickettsia psittaci</i> , virus psittacosisque	-		Birds, mainly parrots and finches	Psittacosis (parrot fe- ver).	0	0	1	See above (174). 179 and 180 : After recovery from the disease, the pathogen can be identified in the blood several years later in the case of birds and up to 10 years later in the case of man. Similar persistence is known only for the pathogens of equine in- fectionous anaemia and of serum hepatitis ³ . For a brief review, see ² .
148	180	Miyagawanella ornithosis spec. nov. RAKE	-		Birds (finches, pheasants, domestic chickens and doves, etc.)	Ornithosis and menin- gopneumonitis.	0	0	1	
148	181	Miyagawanella pneu- moniae spec. nov. RAKE	-		Presumably birds	One of the causes of "virus" pneumonias.	0	0	1	For virus pneumonias, see ⁴ and ⁵ .
148	182	Miyagawanella broncho- pneumoniae MOSHKOVSKY <i>Ehrlichia bronchopneumoniae</i>	-		?	One of the causes of "virus" (broncho-) pneumonias, inc. mouse pneumonitis.	0	0	1	
148	183	Miyagawanella louisianae spec. nov. RAKE	-		?	Louisiana pneumonia.	0	0	1	
148	184	Miyagawanella illinii spec. nov. RAKE	-		?	Illinois pneumonia.	0	0	1	

¹) STOKER, M. G. P., *Brit. med. Bull.*, **9**, 231, 1953. ²) BEDSON, S. P., *Brit. med. Bull.*, **9**, 226, 1953. ³) MACCALLUM, F. O., *Brit. med. Bull.*, **9**, 221, 1953. ⁴) FRUGONI and MAGRASSI, *Sci. med. ital.*, **1**, 203, 1950. ⁵) REIMANN, H. A., *Arch. intern. Med.*, **89**, 115, 1952.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name Synonyms	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks
		Virales ¹⁻⁴ (Antibiotics and chemotherapeutics are without effect, but useful for combating secondary infections and complications.)				
153	185	Variola virus var. hominis, var. bovis <i>Borreliota variolae</i> (LIPSCHÜTZ), Pockenvirus, smallpox virus, <i>Strongyloplasma variolae</i> , virus variolique Cowpox virus, Kuhpocken-Virus, <i>Vaccinia</i> virus (vaccination strain)	Diameter ca. 200 to 300 mμ. Brick-shaped under the electron microscope ⁵ .	<i>Variola</i> : man. <i>Vaccinia</i> : cow, horse. <i>V. bovis</i> : cow.	Smallpox (variola). Vaccination strain. Cowpox.	Cross immunization between all strains of the variola group. Immunity practically life-long. Four distinct strains (cannot or can hardly be distinguished serologically): <i>variola major</i> (mortality 20-30% among non-vaccinated), <i>variola minor</i> (alastrim), <i>Vaccinia</i> (vaccination strain), <i>V. bovis</i> (cowpox; also pathogenic for man, in milkers infection is usually on the hands). Clinically distinguishable, confirmation of diagnosis by culture on chick embryo chorio-allantois ⁶ . Patients become infectious on appearance of the efflorescence. Infection of the foetus in utero on appearance of the first clinical symptoms (fever) ^{7,8} .
153	186	Varicella virus <i>Briareus varicellae spec. nov.</i> , chickenpox virus, Spitzpocken-Virus, Windpocken-Virus		Man.	Chickenpox (varicella).	Encephalitis may accompany varicella. Cf. review ⁹ . Immunity usually life-long, cross immunization against herpes zoster.
153	187	Herpes zoster virus Very probably identical with varicella virus		?	Herpes zoster, shingles, zona.	
153	188	Measles virus <i>Briareus morbillorum spec. nov.</i> , virus rougeoleux		Host: man. Transmitted by direct or close contact with infected persons. The measles virus is very sensitive.	Measles, rubella, morbilli.	Immunity usually life-long. Incubation period 7-21 days.
153	189	Herpes febrilis virus Herpes simplex virus, <i>Neurocystis herpetii</i> LEVADITI and SCHOEN, <i>Scelus recurrens spec. nov.</i>		?	Herpes simplex, herpes febrilis, cause of dendriform keratitis and of aphthous stomatitis.	Primary infection of the child by the mother several months after birth. Subsequent life-long latent infection by the same virus with sporadic outbreaks, often accompanied by bacterial infections. In such cases often regarded as a good sign (pneumonia).
153	190	Virus of warts <i>Molitor verrucae spec. nov.</i> , verrucae virus, virus papillomateux		?	Warts (verrucae).	No immunity.
153	191	Virus of molluscum contagiosum <i>Molitor hominis spec. nov.</i> , <i>Strongyloplasma hominis</i> LIPSCHÜTZ		Contact.	Molluscum contagiosum, acne varioliformis.	
153	192	Virus of sheep encephalitis <i>Erro scoticus spec. nov.</i> , louping ill virus		Transmitted by ticks (<i>Rhipicephalus appendiculatus</i> , <i>Ixodes ricinus</i>).	Sheep encephalitis (louping ill), also pathogenic for man: benign encephalitis.	
153	193	Virus of encephalitis (Russian spring summer) <i>Erro silvestris spec. nov.</i>		Transmitted by ticks (<i>Dermacentor silvarum</i> , <i>Haemaphysalis concinna</i>).	Russian spring summer encephalitis, forest-spring encephalitis, vernal encephalitis.	
153	194	Virus of X-disease <i>Erro incognitus spec. nov.</i>		?	X-disease (Australia): poliо-encephalitis, particularly in children, with high mortality. Late summer.	

¹⁾ RHODES and VAN ROOYEN, *Textbook of Virology*, Baltimore, 1953. ²⁾ BEDSON et al., *Virus and Rickettsial Diseases of Man*, London, 1951. ³⁾ RIVERS, T. M., *Viral and Rickettsial Diseases of Man*, London, 1952. ⁴⁾ *Brit. med. Bull.*, **9**, No. 3, 169-244, 1953. ⁵⁾ DOWNIE and MACDONALD, *Brit. med. Bull.*, **9**, 191, 1953. ⁶⁾ DOWNIE and DUMBELL, *J. Path. Bact.*, **59**, 189, 1947. ⁷⁾ MARSDEN and GREENFIELD, *Arch. Dis. Childh.*, **9**, 309, 1934. ⁸⁾ DIXON, C. W., *J. Hyg. (Lond.)*, **46**, 351, 1948. ⁹⁾ APPELBAUM et al., *Amer. J. Med.*, **15**, 223, 1953.

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks
		Virales¹⁻⁴ (Antibiotics and chemotherapeutics are without effect, but useful for combating secondary infections and complications.) continued				
153	195	Virus of epidemic encephalitis type A			A-encephalitis, lethargic encephalitis, sleeping sickness, ECONOMO's disease, CRUCHET's disease.	Symptomatic diagnosis only in epidemics ⁵⁻⁷ , in sporadic cases confirmation of diagnosis only possible anatomically ⁸ .
153	196	Virus of epidemic encephalitis type B <i>Erro japonicus spec. nov.</i>		?	B-encephalitis, closely related to spring encephalitis (Japan, Russia).	Mortality ca. 8.5%. For description of 300 cases see ⁹ .
153	197	Virus of West Nile encephalitis <i>Erro nili spec. nov.</i>		?	West Nile encephalitis (Uganda).	
153	198	Virus of epidemic encephalitis type C (St. Louis encephalitis) <i>Erro scelestus spec. nov.</i>		Host: practically all warm-blooded animals except rabbits, guinea pigs, rats. Transmitted by mosquitoes (<i>Culex tarsalis</i> , <i>Culex pipiens</i>).	St. Louis encephalitis (America, summer-autumn).	
153	199	Virus of equine encephalomyelitis <i>Erro equinus spec. nov.</i>		Host: practically all warm-blooded animals. Transmitted by mosquitoes, ticks, mites	Equine encephalomyelitis, also pathogenic for man, esp. children (North and South America).	Cf. ¹⁰⁻¹³ and ²⁸ .
153	200	Virus of human poliomyelitis* <i>Legio debilitans spec. nov.</i> , virus of infantile paralysis (Kinderlähmung), Virus poliomyélite		Host: man, excreted in faeces.	Poliomyelitis, infantile paralysis, HEINE-MEDIN disease, acute atrophic paralysis.	For bibliography, see ^{14,15} and on previous page ¹ and ³ . See footnote*.

* Poliomyelitis

Various types and strains exist: of 100 strains examined in USA, 85 were of type *Brunbilde*, 2 of type *Lansing*, 3 of type *Leon*¹⁶. In children the course of the disease usually has two phases, the first commencing with fever, headache, sore throat, loss of appetite, vomiting and apathy. After a remission of several days the second phase follows with fever, headache, muscular pains, stiffness of the limbs, irritability and drowsiness, followed by paralysis¹⁷. Paralysis occurs (when all suspected cases are examined serologically) in only a relatively small proportion of infections, and mainly when infection is followed by a stress of some sort (physical strain, journeys) or after a trauma (tonsillectomy or vaccination with diphtheria toxoid or whooping cough vaccine¹⁸). Such vaccinations should therefore be suspended in the epidemic seasons (particularly late summer and autumn). Pregnancy also predisposes to paralysis¹⁹.

Prophylaxis: Gamma globulin confers protection for a short time (up to ca. 5 weeks), but only when administered before the onset of the first phase. Subsequently it has no significant effect. In USA mass vaccination of children has been adopted following the success of very extensive tests of the SALK poliomyelitis vaccine.

Therapy: tentatively with gamma globulin, using serum of convalescents. *For regression of the paralysis it is very important to start rehabilitation therapy as early as possible.*

** Coxsackie virus group

The Coxsackie group consists of viruses of uniformly high pathogenicity and infectiousness for newborn mice. They are

divided into two subgroups in accordance with the pathological symptoms of the diseases produced in mice: *Group A* cause extensive myositis of the skeletal muscles without other observable lesions; death with flaccid paralysis. *Group B* can also cause a (more localized) myositis, and provoke panniculitis, often also encephalitis; death with spastic paralysis²⁰.

In man the viruses of the Coxsackie group cause infections with a variety of clinical symptoms but which only rarely take a fatal course:

Herpangina (various strains of group A^{21,22}): vesicles and ulcers on tonsils and gums, together with loss of appetite, vomiting, abdominal pains and convulsions. In USA widely distributed in the summer months, especially in children.

Bornholm disease (epidemic pleurodynia) (predominantly strains of group B^{23,24}, but also group A²⁵): severe myalgia, pleurodynia (severe pain in the lower thorax and upper abdomen), fever, pharyngitis and occasionally dry pleurisy.

Aseptic meningo-encephalitis (mainly strains of group B) either accompanying Bornholm disease or as separate syndrome, primarily in northern Europe^{26,27}. Other forms of the disease, such as three-day fever, summer grippe, etc., are probably atypical forms of Bornholm disease, or can simulate non-paralytic poliomyelitis, appendicitis and coronary thrombosis. In years with widespread Coxsackie infections less cases of paralytic poliomyelitis occur.

¹⁻⁴) See page 153. ⁵) v. ECONOMO, C., *Die Encephalitis lethargica*, Vienna, 1929. ⁶) STERN, F., *Die epidemische Encephalitis*, Berlin, 1928. ⁷) PETTE, H., *Die akuten entzündlichen Erkrankungen des Zentralnervensystems*, Leipzig, 1942. ⁸) DÖRING, G., *Münch. med. Wschr.*, **88**, 1053, 1941. ⁹) LINCOLN and SIVERTSON, *J. Amer. med. Ass.*, **150**, 269, 1952. ¹⁰) WENNER et al., *Publ. Hlth Rep. (Wash.)*, **66**, 1075, 1951. ¹¹) SOOTER et al., *Proc. Soc. exp. Biol.*, **77**, 393, 1951. ¹²) MILES et al., *Proc. Soc. exp. Biol.*, **77**, 395, 1951. ¹³) KISSLING et al., *Proc. Soc. exp. Biol.*, **77**, 398, 1951. ¹⁴) FISHBEIN and SALMONSEN (National Foundation for Infantile Paralysis), *A Bibliography of Infantile Paralysis 1789-1949*, London, 1951. ¹⁵) International Poliomyelitis Congress: *Poliomyelitis*, London, 1952. ¹⁶) National Foundation for Infantile Paralysis, Committee on Typing, *Amer. J. Hyg.*, **54**, 191, 1951. ¹⁷) RHODES, A. J., *Brit. med. Bull.*, **9**, 196, 1953. ¹⁸) FABER, H. K., *Pediatrics*, **7**, 300, 1951, and ¹) on previous page. ¹⁹) ANDERSON et al., *Amer. J. Hyg.*, **55**, 127, 1952. ²⁰) TOBIN, J. O'H., *Brit. med. Bull.*, **9**, 201, 1953. ²¹) HUEBNER et al., *New Engl. J. Med.*, **247**, 285, 1952. ²²) KRAVIS et al., *Bact. Proc. (Summary)*, p. 105, 1952. ²³) DISNEY et al., *Brit. med. J.*, **1**, 1351, 1953. ²⁴) WARIN et al., *Brit. med. J.*, **1**, 1345, 1953. ²⁵) WINDORFER and BORN, *Dtsch. med. Wschr.*, **77**, 1012, 1952. ²⁶) GABINUS et al., *Arch. ges. Virusforsch.*, **5**, 1, 1952. ²⁷) OKER-BLOM, N., *Acta path. microbiol. scand.*, Suppl. No. 93, 338, 1952. ²⁸) COHEN et al., *J. Pediat.*, **43**, 26, 1953.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks
		Virales ¹⁻⁴ (Antibiotics and chemotherapeutics are without effect , but useful for combating secondary infections and complications.) continued				
153	201	Coxsackie virus type A type B	Diameter: gradocol, 10-15 mμ; electron microscope, 30-38 mμ.	Host: man, excreted in faeces	Herpangina, Bornholm disease, aseptic meningoencephalitis, summer grippe, three-day fever. See footnote** on previous page.	See footnote** on previous page.
153	202	Virus of lymphocytic choriomeningitis <i>Legio erebea spec. nov.</i>		Experimental transmission by contact and mosquitoes.	Lymphocytic choriomeningitis, often with subclinical course (Europe, USA).	Differential diagnosis from leptospiroses (see page 150).
153	203	Virus of lymphocytic pseudochoriomeningitis <i>Legio simulans spec. nov.</i>		? Patients.	Lymphocytic pseudochoriomeningitis, symptoms identical with choriomeningitis (202). The diseases are not mutually immunizing.	Differential diagnosis from leptospiroses (see page 150).
153	204	Rabies virus <i>Formido inexorabilis spec. nov.</i> , Tollwutvirus, virus rabique		Bite of affected animals (dog, wolf, fox).	Rabies, hydrophobia, lyssa.	Immediate vaccination.
153	205	Yellow-fever virus <i>Charon evegatus spec. nov.</i>	Diameter: 18-27 mμ.	Hosts: man and primates. Transmitted by mosquitoes: man to man cycle mainly by <i>Aedes aegypti</i> (Africa and South America). Apes to man cycle in Africa by <i>A. africanus</i> , <i>A. luteocephalus</i> , <i>A. simpsoni</i> , in South America by <i>A. leucocelaenus</i> and <i>Haemagogus</i> group.	Yellow fever, Bwamba fever (Uganda).	Various strains, with partly atypical, partly benign and partly severe course of the disease. Cross immunization between all strains (also between African and South American yellow fever) ⁵ . An attack confers practically life-long immunity. Prophylaxis: subcutaneous vaccination of adults confers ca. 9 years immunity ⁶ .
153	206	Dengue virus		Transmitted by mosquitoes, esp. <i>Aedes aegypti</i> .	Dengue fever.	Very closely related to yellow-fever virus.
153	207	Virus of Rift Valley fever <i>Charon vallis spec. nov.</i>		Probably transmitted by mosquitoes.	Rift Valley fever, enzootic hepatitis (from cows and sheep). British East Africa, South Africa.	Also pathogenic for man: disease lasts 2-6 days with fever, anorexia, head- and back-ache as main symptoms ⁷ . See brief review in ⁸ .
153	208	Virus of Newcastle disease <i>Tortor furens spec. nov.</i>		Hosts: chickens, man. England, South-east Asia, Australia.	Newcastle disease: in young chickens highly contagious and highly febrile, mainly fatal disease resembling fowl plague.	For epidemic Newcastle disease in man, see ⁹ ; for isolated cases combined with haemolytic anaemia and encephalopathy, see ¹⁰ ; for isolation and identification of the virus, see ¹¹ .
153	209	Virus of foot and mouth disease <i>Hostis pecoris spec. nov.</i> , virus de la fièvre aphteuse, Virus der Maul- und Klauenseuche	Diameter: 6.5-20 mμ	Hosts: artiodactyla: cows, swine, sheep, goats, reindeer, bison, etc. Distributed over the whole world except USA, Australia and New Zealand.	Benign disease with low mortality but which must be energetically combated on economic grounds: infected animals are poor milk and meat producers.	Also, extremely rarely, pathogenic for persons having close contact with cattle. For a brief review, see ⁸ .
153	210	Virus of pappataci fever		Transmitted by sandflies (<i>Phlebotomus papatasi</i>).	Pappataci fever, sandfly fever.	

¹⁻⁴) See page 153. ⁵) DICK, G. W. A., *Brit. Med. Bull.*, **9**, 215, 1953 (includes a review). ⁶) DICK and GEE, *Trans. roy. Soc. trop. Med. Hyg.*, **46**, 449, 1952. ⁷) SMITHBURN et al., *J. Immunol.*, **62**, 213, 1949. ⁸) GLEDHILL, A. W., *Brit. med. Bull.*, **9**, 237, 1953. ⁹) NELSON et al., *Amer. J. publ. Hlth*, **42**, 627, 1952. ¹⁰) MOOLTEN et al., *Amer. J. Med.*, **14**, 294, 1953. ¹¹) BRANDLY et al., *Amer. J. vet. Res.*, **7**, 289, 1946.

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks
		Virales ¹⁻⁴ (Antibiotics and chemotherapeutics are without effect, but useful for combating secondary infections and complications.) continued				
153	211	Influenza virus** type A type B <i>Grippevirus</i> , <i>Tarpeia alpha (beta) spec. nov.</i> , virus grippal		Transmission: contact, droplet infection. World-wide distribution. Host: man.	Influenza, grippe, virus pneumonias.	See footnote**.
153	212	Virus of common cold <i>Tarpeia premens spec. nov.</i>	Diameter: 30-70 mμ.	Transmission: very probably contact, droplet infection. Host: man.	Common cold.	For a brief review, see ⁵ .
153	213	Virus of equine infectious anaemia <i>Trifur equorum spec. nov.</i>		Host: horse.	Also pathogenic for man. World-wide except Australia.	The virus can be identified in the blood 15 years after recovery from the disease. Similar persistence is known only of the agent of psittacosis (10 years) and the virus of serum hepatitis (5 years) ⁶ .

* Cat-scratch disease

The disease occurs in various forms:

A. Typical forms

- 1. Glandular form. Bibliography, see ⁷⁻³⁰.
- 2. Cutaneous form. Bibliography, see ¹⁷.
- 3. Mixed forms.

B. Atypical forms

- 1. Pseudovenereal form. Bibliography, see ³¹.
- 2. Form resembling erythema nodosum. Bibliography, see ³².
- 3. Ocular form. Bibliography, see ³³⁻³⁶.
- 4. Anginose form. Bibliography, see ³⁷.
- 5. Mesenteric form. Bibliography, see ³³.
- 6. Pulmonary form. Bibliography, see ³³.
- 7. Meningo-encephalic form. Bibliography, see ^{33, 38-40}.

** Influenza virus

Very little is as yet known of the epidemiology of influenza. Type A causes widespread epidemics every 2-3 years. These are usually more dangerous than the annual sporadic localized epidemics of type B. No other infectious disease can spread so rapidly over the whole world or cause, particularly among older persons, such a high death rate. During epidemics an incidence of 5-10% must be reckoned with, without counting subclinical infections. Prophylactically only vaccination is of any value. For a short review, see ⁴¹.

*** Hepatitis virus

Clinically there is practically no difference in the hepatitis caused by the two strains of this virus. Although the view is sometimes expressed that both infective and haematogenic hepatitis are caused by the same organism⁴², it is generally accepted that there are two distinct strains with the following differing characteristics⁶:

	Infective hepatitis Virus A	Serum hepatitis Virus B
Incubation period	15-40 days	60-160 days
Virus in faeces	during the acute phase	not identified
Virus in blood	3 days before commencement and in the acute phase	whole incubation period and acute phase
Route of infection (experimental)	oral and parenteral	parenteral only
Homologous immunity	certain (almost life-long)	apparently none
Heterologous immunity	apparently none	apparently none
Prophylactic value of gamma globulin	good	variable
Latent stage (blood)	unknown	up to 5 years

The long-persisting latent stage of the serum-hepatitis virus is of great interest. Similar long latent stages after recovery from the disease are known only in the cases of the pathogens of psittacosis (179) and equine infectious anaemia (213). On hepatitis virus see ⁴³, for a brief review see ⁶.

¹⁻⁴) See page 153. ⁵) ANDREWES, C. H., *Brit. med. Bull.*, **9**, 206, 1953. ⁶) MACCALLUM, F. O., *Brit. med. Bull.*, **9**, 221, 1953. ⁷) ANDRÉ and DREIFUSS, *Bull. Soc. méd. Hôp. Paris*, **68**, 157, 1952. ⁸) BORIOLI and BADARACCO, *Praxis*, **13**, 263, 1952. ⁹) DANIELS and MACMURRAY, *Arch. intern. Med.*, **88**, 736, 1951. ¹⁰) DEBRÉ et al., *Bull. Soc. méd. Hôp. Paris*, **66**, 76, 1950; *ibid.*, **66**, 1895, 1950. ¹¹) DENÉCHAU, D., *Bull. Soc. méd. Hôp. Paris*, **68**, 347, 1952. ¹²) SPIRIDON, D., *Diss.*, Geneva, 1951. ¹³) GARAI, O. F., *Lancet*, **1**, 646, 1952. ¹⁴) GREER and KEEFER, *New Engl. J. Med.*, **244**, 545, 1951. ¹⁵) GSELL et al., *Schweiz. med. Wschr.*, **81**, 699, 1951. ¹⁶) HEDINGER, CHR., *Virchows Arch. path. Anat.*, **322**, 159, 1952. ¹⁷) HEDINGER et al., *Dermatologica*, **104**, 101, 1952. ¹⁸) KAPLAN et al., *Bull. Soc. méd. Hôp. Paris*, **66**, 852, 1950. ¹⁹) LEMAIRE and DEBRAY, *Bull. Soc. méd. Hôp. Paris*, **66**, 375, 1950. ²⁰) MAHOUDEAU et al., *Bull. méd. Hôp. Paris*, **66**, 420, 1950. ²¹) MOLLARET et al., *Bull. Soc. méd. Hôp. Paris*, **66**, 424, 1950. ²²) MOLLARET et al., *Presse méd.*, **58**, 282, 1353, 1950; *ibid.*, **59**, 681, 701, 1951. ²³) PAGÈS et al., *Bull. Soc. méd. Hôp. Paris*, **67**, 213, 1951. ²⁴) PARAF and FOURNIER, *Bull. Soc. méd. Hôp. Paris*, **66**, 539, 1950. ²⁵) SCHÜRMANN and REICH, *Klin. Wschr.*, **30**, 366, 1952. ²⁶) SIGUIER et al., *Bull. Soc. méd. Hôp. Paris*, **67**, 571, 1951. ²⁷) THOMAS et al., *Ophthalmologica*, **123**, 129, 1952. ²⁸) USTERI and HEDINGER, *Schweiz. med. Wschr.*, **81**, 221, 1951. ²⁹) WEGMANN et al., *Schweiz. med. Wschr.*, **81**, 853, 1951. ³⁰) WILLCOX, R. R., *Lancet*, **1**, 673, 1952. ³¹) SIGUIER et al., *Bull. Soc. méd. Hôp. Paris*, **68**, 216, 1952. ³²) WEILL and BLAS, *Bull. Soc. méd. Hôp. Paris*, **67**, 1141, 1951. ³³) USTERI et al., *Schweiz. med. Wschr.*, **82**, 1287, 1952. ³⁴) DE LAVERGNE et al., *Bull. Soc. méd. Hôp. Paris*, **67**, 985, 1951. ³⁵) THÉLIN and DU PAN, *Praxis*, **40**, 74, 1951. ³⁶) CLÉMENT et al., *Bull. Soc. méd. Hôp. Paris*, **67**, 1108, 1951. ³⁷) MOLLARET et al., *Bull. Soc. méd. Hôp. Paris*, **67**, 565, 1951. ³⁸) GROSSIORD et al., *Presse méd.*, **60**, 816, 1952. ³⁹) DEPAILLAT and CONDAT, *Presse méd.*, **60**, 631, 1952. ⁴⁰) ROZET and FAU, *Presse méd.*, **60**, 41, 1952. ⁴¹) ISAACS, A., *Brit. med. Bull.*, **9**, 208, 1953. ⁴²) ESSEN and LEMBKE, *Zbl. Bakt., I. Abt. Orig.*, **159**, 387, 1953. ⁴³) World Health Organization, Expert Committee on Hepatitis, *Wld Hlth Org. techn. Rep. Ser.*, **62**, 1953.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks
		Virales¹⁻⁴ (Antibiotics and chemotherapeutics are without effect , but useful for combating secondary infections and complications.) continued				
153	214	Hepatitis virus Type A: virus of infective hepatitis		Excreted in faeces.	Infective hepatitis.	See footnote*** on previous page.
153	215	Hepatitis virus Type B: virus of serum hepatitis		Transmitted by blood or serum of others, by infected hypodermic needles.	Inoculation hepatitis, haemato-genic hepatitis.	
153	216	Cat-scratch virus		Transmitted through scratches from cats' claws.	Cat-scratch disease, cat-scratch lymphadenitis, lymphoreticulosis benigna.	The disease takes various forms; see footnote* on previous page.
153	217	Virus of Manchurian fever Virus of epidemic haemorrhagic fever, Mandschurien-fieber-Virus		Probably transmitted by ticks	Manchurian fever, mortality ca. 20% of cases (Korean war).	Cf. ⁵ .
153	218	Mumps virus <i>Rabula inflans spec. nov.</i>		Contact.	Mumps epidemic, parotitis, mumps-orchitis, -meningo-encephalitis, -pancreatitis, and other rarer localizations.	An attack confers practically life-long immunity. For a brief review, see ⁶ .
		Protozoa				
154	219	Entamoeba histolytica SCHAUDINN <i>Amoeba coli</i> , <i>Caudamoeba sinensis</i> , <i>Entamoeba africana</i> , <i>Entamoeba dysenteriae</i> , <i>Entamoeba minuta</i> , <i>Entamoeba nuttalli</i> , <i>Entamoeba schaudinni</i> , <i>Entamoeba tetragena</i> , <i>Entamoeba urogenitalis</i>	Diameter: (10-) 20-30 μ m, usually 4 nuclei.	Host: man. Transmission: ingestion of cysts (contaminated water or food, above all salads). World-wide distribution, inc. temperate zones.	A. Intestinal amoebiasis: 1. <i>Asymptomatic</i> , ca. 90% of carriers (temperate zones) ^{7,8} . 2. <i>Non-dysenteric amoebiasis</i> , with obscure abdominal pains, flatulence, nausea, fatigability, headache, nervousness ⁹ . 3. <i>Amoebic dysentery</i> . B. Metastatized (intestinal) amoebiasis: predominantly hepatitis, in a very few cases hepatic abscesses, more rarely lung and brain abscesses. For a brief review, see ¹⁰ .	Intestinal amoebiasis. Antibiotics of choice: tetracyclins. Initial dose 2 g (30 grains), then 0.25-0.5 g (4-8 grains) 4 times daily for 10 days. The action of the tetracyclins is probably not direct but due to destruction of bacteria essential to the growth of the amoebae. Metastatized amoebiasis (hepatitis, abscesses). Antibiotic of choice: chloroquine diphosphate. Dose 0.5 g (8 grains) twice daily for 2 days, then 0.5 g once daily for 2-3 weeks. For other amoebicides see ¹¹ . The cure should always be repeated. For bibliography on amoebiasis, see ¹²⁻²¹ .
154	220	Entamoeba coli (LOESCH) SCHAUDINN <i>Amoeba intestini vulgaris</i> , <i>Entamoeba hominis</i> , <i>Entamoeba nipponica</i> , <i>Entamoeba williamsi</i>	Diameter: 10-30 μ m, usually 8 nuclei.	Host and transmission: see above (219).	Usually non-pathogenic. World-wide distribution, ca. 50% of all individuals.	
154	221	Entamoeba gingivalis GROS <i>Amoeba buccalis</i> , <i>Amoeba dentalis</i> , <i>Entamoeba confusa</i> , <i>Entamoeba macrohyalina</i>	Diameter: 12-20 μ m, 1 nucleus.	Host: man. Transmitted by close contact (kissing, etc.).	Non-pathogenic, except for possible increase of alveolar sup-puration. Not a normal mouth saprophyte.	Chloroquine ineffective.

¹⁻⁴) See page 153: ⁵) MONROE, B. B., *N. C. med. J.*, **13**, 91, 1952. ⁶) SPOONER, E. T. C., *Brit. med. Bull.*, **9**, 212, 1953. ⁷) CRAIG, C. F., *Amebiasis and Amebic Dysentery*, Springfield, 1934. ⁸) CRAIG, C. F., *J. Parasit.*, **22**, 1, 1935. ⁹) SAPERO, J. J., *Amer. J. trop. Med.*, **19**, 255, 497, 1939. ¹⁰) KUNERT and MIRECKI, *Arztl. Wschr.*, **7**, 929, 1952. ¹¹) ELSON and ROGERS, *Med. Clin. N. Amer.*, **37**, 1803, 1953. ¹²) HARGREAVES, W. H., *Lancet*, **2**, 68, 1945. ¹³) ARMSTRONG et al., *Trans. roy. Soc. trop. Med. Hyg.*, **42**, 597, 1949. ¹⁴) MOST, H., *Bull. N. Y. Acad. Med.*, **25**, 717, 1949. ¹⁵) MOST et al., *Amer. J. trop. Med.*, **30**, 491, 1950. ¹⁶) MOST et al., *J. Amer. med. Ass.*, **143**, 792, 1950. ¹⁷) MOST and VAN ASSENDELLET, *Ann. N. Y. Acad. Sci.*, **53**, 427, 1950. ¹⁸) JONES, W. R., *Nature*, **165**, 649, 1950. ¹⁹) McVAY et al., *Sth. med. J.*, **43**, 308, 1950. ²⁰) HUGHES, I. D., *J. Amer. med. Ass.*, **142**, 1052, 1950. ²¹) SHOOKHOFF, H. B., *Bull. N. Y. Acad. Med.*, **27**, 439, 1951.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks Antibiotics Chemotherapeutics
		Protozoa - continued				
154	222	Endolimax nana WENYON et O'CONNOR <i>Amoeba limax</i>	Diameter 6-12 µm, usually 4 nuclei.	Host and transmission, see 219 on previous page.	Non-pathogenic, present in 15 to 30% of all individuals.	Chloroquine variably effective.
154	223	Pseudolimax bütschlii PROWAZEK <i>Endolimax pileonucleatus</i> , <i>Endolimax williamsi</i> , <i>Iodamoeba bütschlii</i> , <i>Iodamoeba williamsi</i> , <i>Pseudolimax wenyoni</i>	Diameter 9-11 µm, 1 nucleus.	Host and transmission, see 219 on previous page.	Very probably non-pathogenic, present in only 2-6% of individuals, in swine 20-50%.	As for 219 and 222.
154	224	Dientamoeba fragilis JEPPS et DOBELL	Diameter 5-12 µm, usually 2 nuclei, sometimes 1 only.	Host and transmission, see 219 on previous page.	Definitely pathogenic, 1-2% of all amoebiasis cases.	As for 219 and 222.
155	225	Cercomonas crassicaudia DUJARDIN	Length 5-10 µm, 2 flagella.	Faeces (not intestine).	Non-pathogenic.	Pass through the intestinal tract as cysts.
155	226	Embadomonas intestinalis WENYON et O'CONNOR	Length 4-9 µm, 2 flagella.	Large intestine, very rare.	Non-pathogenic.	
156	227	Bodo caudatus DUJARDIN <i>Bodo asiaticus</i> , <i>Bodo urinaris</i> , <i>Prowazekia cruzi</i>	Length 5-10 µm, 2 flagella.	Faeces (not intestine).	Non-pathogenic.	Pass through the intestinal tract as cysts.
156	228	Enteromonas hominis <i>Tricercomonas intestinalis</i>	Length 4-10 µm, 4 flagella.	Large intestine, rare.	Non-pathogenic.	
157	229	Trypanosoma gambiense DUTTON <i>Trypanosoma castellani</i> , <i>Trypanosoma fordi</i> , <i>Trypanosoma hominis</i> , <i>Trypanosoma lanfranchii</i> , <i>Trypanosoma neprevi</i> , <i>Trypanosoma ugandense</i>	Length 15-30 µm.	Transmitted by tsetse flies: <i>Glossina palpalis</i> and <i>Glossina tachinoides</i> .	African sleeping sickness: tropical West Africa to Uganda. The <i>T. gambiense</i> infection runs a milder course than <i>T. rhodesiense</i> and is more responsive, at least in the early stages, to treatment with the currently available drugs.	Arsenicals such as tryparsamide or aromatic diamidines.
157	230	Trypanosoma rhodesiense STEPHENS et FANTHAM	Length 15-30 µm.	Transmitted by tsetse flies: <i>Glossina morsitans</i> and <i>Glossina swynnertoni</i> (cf. 229).	African sleeping sickness: East Africa (Kenya to Southern Rhodesia and northern Mozambique) to Tanganyika, Uganda and eastern Congo. The <i>T. rhodesiense</i> infection runs a much more rapid course than <i>T. gambiense</i> and if untreated results in death in 3-4 months.	As for <i>Trypanosoma gambiense</i> (229).
157	231	Schizotrypanum cruzi CHAGAS <i>Trypanosoma cruzi</i> , <i>Trypanosoma escomeli</i> , <i>Trypanosoma neotomae</i> , <i>Trypanosoma rhesi</i> , <i>Trypanosoma vickersae</i>	Length ca. 20 µm.	Hosts: <i>Triatoma</i> (<i>T. megista</i> , <i>heidemanni</i> , <i>infestans</i> , <i>longipes</i> , <i>gerstaeckeri</i> , <i>protracta</i> , <i>rubida</i> , <i>sanguisuga</i> , <i>ambigua</i> , etc.) and <i>Rhodnius prolixus</i> etc., <i>Erathyr</i> a and <i>Amblyomma longirostre</i> .	CHAGAS' disease: South America. Affects mainly debilitated individuals and children. Occurs principally in crop areas, such as Minas Gerais in Brazil.	The trypanosomacides mentioned under 229 above are ineffective; up to the present no certain agent has been found.
157	232	Leishmania donovani LAVERAN et MESNIL	Diameter 2-4 µm, round or oval.	Transmitted probably by sandflies (phlebotoma).	Kala-azar (visceral leishmaniasis, Dumdum fever), particularly in India (Assam, Bengal, Bihar), northern China, Sudan.	Antimonials: tartar emetic, stibamine, neostibosan; also arsenicals such as neosalvarsan. Antibiotics ineffective.
157	233	Leishmania infantum	As above (232).	Transmitted probably by sandflies (phlebotoma) and the dog flea (<i>Ctenocephalides canis</i>).	Mediterranean (infantile) kala-azar (leishmaniasis), mainly in children (esp. under 3 years): Mediterranean area.	As above (232).
157	234	Leishmania tropica WRIGHT <i>Leishmania furunculosa</i>	As above (232).	Transmitted by flies and contact.	Mucocutaneous leishmaniasis in Asia Minor and India (Aleppo boil, oriental button, Delhi sore, tropical ulcer, etc.).	As above (232), plus local treatment.
157	235	Leishmania brasiliensis VIANNA <i>Leishmania braziliensis</i> , <i>Leishmania peruviana</i>	As above (232).	As above (234).	Mucocutaneous leishmaniasis of tropical America (Bahia boil, espundia).	As above (232), plus local treatment.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name Synonyms	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks Antibiotics Chemotherapeutics
		Protozoa - continued				
158	236	Trichomonas intestinalis LEUCKART <i>Monocercomonas hominis</i> , <i>Pentatrichomonas ardin-delteili</i> (with 5 flagella), <i>Trichomonas hominis</i>	Length 8-12 μ m, 4 or 5 flagella.	Large intestine.	Pathogenicity uncertain, occasionally associated with diarrhoea.	Tetracyclins orally.
158	237	Trichomonas vaginalis* DONNÉ	Length (10) 15-(20) 30 μ m, 4 flagella.	Vagina, also urethra (both sexes), occasionally in cervix and prostate.	See footnote*.	See footnote*.
158	238	Trichomonas elongata STEINBERG <i>Trichomonas buccalis</i> , <i>Trichomonas tenax</i>	Length 6-10 μ m.	Mouth-cavity.	Pathogenicity doubtful, present in 22-40% of all individuals.	
158	239	Chilomastix mesnili WENYON <i>Cercomonas hominis</i> , <i>Chilomastix granatensis</i> , <i>Cyathomastix hominis</i> , <i>Difoemus tunensis</i> , <i>Fanapepea intestinalis</i> , <i>Macrostoma mesnili</i> , <i>Tetramitus mesnili</i>	Length (6) 10-(15) 20 μ m, 3 flagella.	Large intestine.	Non-pathogenic.	
159	240	Giardia intestinalis LAMBL <i>Cercomonas intestinalis</i> , <i>Giardia enterica</i> , <i>Hexamitus duodenalis</i> , <i>Lamblia intestinalis</i> , <i>Megastoma entericum</i> , <i>Megastoma intestinale</i>	Diameter 10-18 μ m, 8 flagella, 2 nuclei.	Small intestine, occasionally bile duct and gallbladder.	Occasionally asymptomatic, usually pathogenic (lambliaosis). The thick layer of lamblia on the mucosa interferes mainly with fat resorption, thus causing symptoms similar to coeliac disease, sprue or chronic gallbladder affections.	Mepacrine (quinacrine) or glycolyl arsanilate (both orally).
161	241	Toxoplasma (cuniculi, canis, avium)**	Diameter 3-6 μ m.	Host: dogs, rats, mice, rabbits, birds.	See footnote**.	Sulphonamides have a certain effect (in the acute form). Antibiotics are ineffective.

*** Trichomonas vaginitis**

The pathogenicity of *Trichomonas vaginalis* is still in doubt. There are three opinions on this subject:

1. *Trichomonas* is pathogenic. This view is supported by experiments¹ in which a typical trichomonas vaginitis was produced by inoculation with bacteria-free cultures of *Trichomonas*.
2. *Trichomonas* is only pathogenic in symbiosis with certain bacteria or viruses. This view is strongly supported by the fact that a disturbance of the bacterial flora (grade III) is found in practically all cases of manifest trichomonas vaginitis.
3. *Trichomonas* is a saprophyte, which finds itself in an improved environment as a result of a vaginitis caused by some particular bacterium and is thus enabled to multiply enormously. It is therefore characteristic of the fluor as apparent aetiological factor, without in fact being itself pathogenic.

Of these three views the second is probably the most likely since *Trichomonas* is often found to be present on persons without corresponding clinical manifestations and, furthermore, trichomonas vaginitis responds readily to the tetracyclins, which are normally effective against bacteria but ineffective against protozoa.

Therapy: tetracyclins locally applied; it is advantageous to administer orally also at the start of treatment in view of localizations difficult of access (urethra, glands of BARTHOLIN, cervix). The treatment should be repeated at intervals. The patient should be kept under observation particularly during menstruation and pregnancy. Along with the locally applied tetracyclins the use of a fungicide is recommended (preferably the methyl or propyl ester of parahydroxybenzoic acid) in order to eliminate the danger of a mycotic superinfection. Concomitant and subsequent therapy is directed to restoring as rapidly as possible the normal bacterial flora. Parallel examination and, where necessary, treatment of the husband is absolutely indicated.

For a review of vaginal infections including trichomoniasis, see ².

For a review and bibliography of urogenital trichomoniasis in men, see ³.

**** Toxoplasmosis⁴⁻⁸**

Clinical symptoms of the congenital form: chorioretinopathy, cerebral calcification, hydrocephaly or microcephaly, psychomotor disturbances. 80-90% of such syndromes are caused by *Toxoplasma*.

In adults various groups of symptoms are found:

1. Central-nervous form with aseptic meningitis, encephalomeningitis.
2. Forms with cutaneous manifestations: maculopapular exanthema (acute stage) or cutaneous and subcutaneous perivascular infiltrates (chronic stage), resembling erythema nodosum.
3. Pulmonary symptoms resembling interstitial pneumonia, with peculiar eosinophil, perialveolar infiltrates.
4. Ophthalmic diseases in the form of choroiditis, choroidoretinitis, opacity of the vitreous, conjunctivitis. In addition, frequently fever, arthralgia, myalgia and lymphadenitis. In contrast to infantile (congenital) toxoplasmosis, cerebral calcification does not occur and choroidoretinitis is rare.

Course: either latent and asymptomatic, or with acute commencement with fever and the symptoms described above, or chronic with occasional acute outbreaks. With the exception of very mild infections, usually fatal.

Diagnosis: symptomatic, confirmed by identification of the pathogen (cerebrospinal fluid) or of the antibodies. The latter in any case appear only at a very late stage or not at all.

¹) TRUSSEL and PLASS, *Amer. J. Obstet. Gynec.*, **40**, 833, 1940. ²) BERNSTEIN and RAKOFF, *Vaginal Infestations and Discharges*, New York, 1953. ³) BAUER, H., *Fortschr. Med.*, **71**, 397, 1953. ⁴) SABIN and FELDMAN, *J. Paediat.*, **35**, 296, 1949. ⁵) SABIN et al., *J. Amer. med. Ass.*, **150**, 1063, 1952. ⁶) WOLLHEIM, E., *Munch. med. Wschr.*, **94**, 193, 1952. ⁷) KASS et al., *Arch. intern. Med.*, **89**, 759, 1952. ⁸) VALENTINE et al., *J. clin. Path.*, **6**, 253, 1953.

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks Antibiotics Chemotherapeutics
		Protozoa - continued				
162	242	Plasmodium vivax* GRASSI et FELETTI <i>Haemamoeba vivax</i> , <i>Plasmodium tertianae</i>	Interval between sporulations: 48 hours.	Intermediate host and transmitter: mosquitoes: <i>Anopheles claviger</i> (<i>maculopennis</i>), <i>A. bifurcatus</i> , <i>A. superpictus</i> , <i>A. pseudo-pictus</i> , <i>A. gambiae</i> .	Malaria: tertian benign form.	See footnote*.
162	243	Plasmodium malariae* LAVERAN <i>Haemamoeba malariae</i> , <i>Oscillaria malariae</i> , <i>Plasmodium quartanae</i>	Interval between sporulations: 72 hours.	As above (242).	Malaria: quartan form.	See footnote*.
162	244	Plasmodium falciparum* WELCH <i>Haemamoeba praecox</i> , <i>Laverania malariae</i> , <i>Laverania praecox</i> , <i>Plasmodium immaculatum</i> , <i>Plasmodium praecox</i> , <i>Plasmodium quotidianum</i> , <i>Plasmodium tenue</i>	Interval between sporulations: 48 hours.	As above (242).	Malaria: tropical form (tertian malignant, estivo-autumnal). Black-water fever is probably closely related to tropical malaria.	See footnote*.
169	245	Balantidium coli MALMSTEN <i>Balantidium giganteum</i>	Length 60-100µm, breadth 50-70µm.	Intestines of swine.	Pathogenic: chronic dysentery, often with fatal evolution.	The tetracyclins have a limited effect <i>in vitro</i> .

* Malaria and chemotherapeutics

Although still one of the most important of infectious diseases, affecting populations over large areas, malaria can be effectively and rationally combated with the chemotherapeutic agents now available (hygienic methods of control will not be dealt with here). A short description of the **life-cycle of the Plasmodia** is appropriate to an explanation of the use of these agents:

Host I: man.

1st Phase: *tissue phase*†. As a result of the bite of an infected mosquito, the sporozoites enter the blood stream and after a short interval disappear into the tissues. The tissue phase causes no clinical symptoms.

2nd Phase: *blood phase*.

- a) Asexual blood phase. After a short latent period (several days to a week) the trophozoites produced in the tissues pass into the blood stream and invade the erythrocytes. Here they undergo parthenogenetic multiplication (schizogenesis) at certain definite intervals (depending on the species, see above). This schizogonic phase is responsible for the principal clinical symptoms (feverish attacks, etc.).
- b) Sexual blood phase. After the schizogonic phase the trophozoites develop finally into the sexual gametocytes. These circulate for a long time in the blood stream and can there likewise reproduce themselves parthenogenetically, without, however, causing clinical symptoms.

Host II: mosquitoes. When the gametocytes enter a mosquito they copulate and develop finally into sporozoites, whereby the cycle is completed when the latter are again transmitted to man.

In the **falciparum infection** the tissue phase produces only

† The existence of a tissue phase has not yet been proved with certainty but the clinical course of malaria and the efficacy of chemotherapeutics point very strongly towards one.

one batch of trophozoites, after which it dies out or becomes unproductive: this infection is short-lived and there is no recidivism (except by reinfection). Chemotherapeutic destruction of the schizogonic phase (asexual blood phase), the only active phase, thus terminates a falciparum infection immediately, even when the agent is absolutely ineffective with regard to the tissue phase.

In contrast to this, the tissue stage of **vivax malaria** establishes itself as a chronic condition which if untreated can last for years. It is only gradually attenuated by immunobiological processes. At intervals of several weeks or more this persistent tissue stage continues to produce fresh batches of trophozoites which are the cause of the many relapses of a vivax infection. The development of vivax malaria takes two distinct courses: the *tropical form* (India, south-west Pacific, tropical America, equatorial Africa, Mediterranean, Rome) shows a short latent period of about one week between the first attack and the subsequent first relapse, after which further relapses follow fairly regularly at the above-mentioned intervals.

The *temperate-zone form* (Macedonia, northern Italy, Holland, central Russia, temperate America, Madagascar, Korea) is characterized by a long latent period of 6-10 months between the first attack and the first relapse, the subsequent relapses then following, as in the tropical form, regularly at shorter intervals. Here it appears to be a case of adaptation of the Plasmodia life-cycle to a season unfavourable to transmission by mosquitoes.

In contrast to falciparum malaria, the vivax infection is therefore not amenable to treatment by chemotherapeutics which destroy only the schizogonic phase of Plasmodia, and only the clinical symptoms of the attacks can be eliminated by this means. The avoidance of further relapses and the final eradication of the infection require either an agent which can be relied upon to destroy simultaneously both the tissue and schizogonic phases (such an agent has not yet been discovered) or the use of two chemotherapeutics each of which is specific for one of these two phases.

(continued on the opposite page)

¹⁾ Council on Pharmacy and Chemistry, Report to the Council, *J. Amer. med. Ass.*, **149**, 1952: STORMONT, R. T., p. 1558; GARRISON et al., p. 1562; CLAYMAN et al., p. 1563; HOCKWALD et al., p. 1568. ²⁾ SINGH and KALYANUM, *Brit. med. J.*, **2**, 312, 1952. ³⁾ HOEKENGA et al., *J. Amer. med. Ass.*, **149**, 1369, 1952. ⁴⁾ ALVING et al., *Amer. J. trop. Med. Hyg.*, **2**, 970, 1953. ⁵⁾ JONES et al., *Amer. J. trop. Med. Hyg.*, **2**, 977, 1953. ⁶⁾ DI LORENZO et al., *Amer. J. trop. Med. Hyg.*, **2**, 983, 1953. ⁷⁾ COATNEY et al., *Amer. J. trop. Med. Hyg.*, **2**, 985, 1953. ⁸⁾ LOVE et al., *Amer. J. med. Sci.*, **225**, 26, 1953. ⁹⁾ COOPER et al., *Amer. J. trop. Med. Hyg.*, **2**, 949, 1953. ¹⁰⁾ EDGCOMB et al., *J. nat. Malar. Soc.*, **9**, 285, 1950.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name Synonyms	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks Antibiotics Chemotherapeutics
		(In the case of the helminths the term "infestation" has been used in place of "infection"; the term is understood to signify infections in which the parasite does not multiply in the body of the host. An infestation usually only becomes dangerous when the parasites penetrate or are carried into the organism in large numbers.)				
174	246	Fasciolopsis buski LANKESTER <i>Distomum buski</i> , <i>Distomum crassum</i> , <i>Fasciolopsis fülleborni</i> , <i>Opisthorchis buski</i>	Length 2-7.5 mm.	Intermediate host: water snails of the genus <i>Segmentina</i> . Host: man, swine, dogs, goats. Infestation: by ingestion of cyst-infected aquatic plants (<i>Trapa natans</i> in China, <i>T. bicornis</i> in East Bengal) and the water-chestnut (<i>Eleocharis tuberosa</i>).	In China and some localities of India infestation with <i>F. buski</i> is everywhere endemic where these plants are eaten extensively.—The worm infests the small intestine, causes local inflammation and secretes toxins: bloody diarrhoea, severe anaemia, finally ascites and oedema on limbs and face. Can result in death.	Prompt elimination by hexylresorcinol, thymol, carbon tetrachloride and chenopodium oil. On <i>Fasciolopsis</i> see ¹⁻³ and ⁹ .
174	247	Paragonimus ringeri COBBOLD <i>Distoma pulmonale</i> , <i>Mesogonimus westermanni</i> , <i>Paragonimus westermanni</i>	Length 8-12 mm, breadth 4-6 mm.	1st intermediate host: snails (<i>Melania libertina</i> in the East, <i>Pomatopsis lapidaria</i> in USA, and others). 2nd intermediate host: crabs and crayfish. Final host (normal): cats, dogs, swine. Infestation: ingestion of infected crabs or crayfish.	Endemic in the East, particularly in Japan, sporadic in North America. <i>Paragonimus</i> infests the lungs and the symptoms recall those of tuberculosis (blood in sputum) but are not severe. Infestation of the brain leads to symptoms resembling epilepsy and brain tumours and is fatal. With lung infestations healing takes 5-6 years if no re-infestation occurs.	No definitely effective agent is known. Good results have been observed with antimonials (parenteral) and with combinations of sulphonamides and emetine. On <i>Paragonimus</i> see ⁴ for China and ⁵ for America.
174	248	Clonorchis sinensis COBBOLD <i>Distomum sinense</i> , <i>Distomum spatulatum</i> , <i>Clonorchis endemicus</i> , <i>Opisthorchis sinensis</i>	Length 10-25 mm, breadth 3-5 mm.	1st intermediate host: snails, esp. <i>Parafossalurus striatulus</i> . 2nd intermediate host: carp (<i>Cyprinidae</i>). Final host: dogs, cats, man where raw fish is eaten.	Everywhere in the East, esp. Japan, Canton, Indochina. Infests the bile ducts, occasionally also the pancreatic ducts. Mild infestation is asymptomatic; severe infestation causes diarrhoea (often bloody), oedema, enlargement of the liver, anaemia.	No certain remedy. In the early stages good results are shown by gentian violet and related dyes. On <i>Clonorchis</i> (<i>Opisthorchis</i>) see ⁶⁻⁸ .

Malaria and chemotherapeutics (continued)

In this connection the antimalarials at present available can be grouped as follows:

1. Effective on tissue phase (curative agents):

Primaquine: preferred agent from the point of view of efficacy, toxicity and ease of administration
Chlorguanide
2. Effective on schizonts (asexual blood phase) (suppressive agents):

Chloroquine in first place†
Amodiaquine in second place†
followed by
Chlorguanide
Quinacrine (Mepacrine)
Oxychloroquine
Quinine
3. Effective on gametocytes (sexual blood phase):

Primaquine
Pamaquine
Pentaquine and isopentaquine

The names given above are the trivial names in use in Great Britain and USA; there should be no difficulty in finding the appropriate trade names. The systematic names are given at the end of this footnote.

In accordance with the foregoing, the most effective antimalarial treatment in the light of present-day knowledge is as follows:

† If the efficacy of a single dose is regarded as the criterion, then this evaluation should be reversed, i.e. amodiaquine is superior to chloroquine.

Falciparum infections

Chloroquine: 1st day, 1 × 0.6-1 g (9-15 grains); on each of the two following days, 2 × 0.3 g (5 grains); subsequently 1 × 0.5 g (8 grains) weekly for 2-3 weeks.

or

Amodiaquine: one single dose of 0.01 g (10 mg) per kg body-weight (5 mg per lb. body-weight) (about 20% of failures).

Vivax infections

Combination therapy with chloroquine or amodiaquine (dosage as for falciparum infections) plus primaquine for 14 days with a daily dose of 0.01-0.03 g (10-30 mg), average 0.015 g (15 mg), according to the degree of immunity of the patient. In general 0.015 g suffices, with negroes 0.02 g should not be exceeded.

Prophylactically, for suppression of fever attacks in malarial areas: weekly 1 × 0.5 g (8 grains) chloroquine.

Chemical terminology

Amodiaquine = 7-chloro-4-(3'-diethylaminomethyl-4'-hydroxyanilino)quinoline. Chlorguanide = N¹-p-chlorophenyl-N⁵-isopropylbiguanide. Chloroquine = 7-chloro-4-(4'-diethylamino-1'-methyl)butylaminoquinoline. Pamaquine = 6-methoxy-8-(1'-methyl-4'-diethylamino)butylaminoquinoline. Pentaquine = 6-methoxy-8-(5'-isopropylamino)pentylaminoquinoline. Primaquine = 6-methoxy-8-(4'-amino-1'-methyl)butylaminoquinoline. Quinacrine = 2-chloro-5-(1'-methyl-4'-diethylamino)butylamino-7-methoxyacridine.

¹) BARLOW, C. H., *Amer. J. Hyg. Monogr. Ser.* 4, 1925. ²) VOGEL, H., *Arch. Schiffs- u. Tropenhyg.*, 40, 181, 1936. ³) WU, K., *Ann. Parasit. hum. comp.*, 15, 458, 1937. ⁴) WU, K., *Far Eastern Ass. trop. Med. Compt. rend.* 10^e Congrès, Hanoi, 1938. ⁵) AMIEL, D., *Amer. J. Hyg.*, 19, 279, 1934. ⁶) VOGEL, H., *Zoologica*, 33, 86, 1934. ⁷) HSU et al., *Chin. med. J.*, 50, 1609, 1936; *ibid.*, Suppl. 2, 385, 1938; *ibid.*, Suppl. 3, 234, 1940. ⁸) CAMERON, T. W. M., *Canad. J. Res.*, 22, 6, 1944. ⁹) SADUN and MAIPHOOM, *Amer. J. trop. Med. Hyg.*, 2, 1070, 1953.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks Antibiotics Chemotherapeutics
174	249	Platyhelminthes - continued Metagonimus yokogawai KATSURADA <i>Heterophyes yokogawai</i> , <i>Loxotrema ovatum</i> , <i>Paragonimus yokogawai</i> , <i>Yokogawa yokogawai</i>	Length 1-2.5 mm, breadth ca. 0.5 mm.	1st intermediate host: snails of genus <i>Melania</i> ; 2nd intermediate host: fresh-water fish (trout variety, esp. <i>Plecoglossus altivelis</i>). Final host: carnivores, esp. cats, dogs and, where raw fish is eaten, man.	Widespread in Japan, Philippines and eastern Siberia. Infests the duodenum, causes no clinical symptoms, and can be regarded as a "normal" parasite. Severe infestation can lead to mild digestive troubles and diarrhoea.	Chenopodium oil, thymol, santonin, carbon tetrachloride, hexylresorcinol, after thorough colonic washing. On <i>Metagonimus</i> see ¹ and ² .
174	250	Heterophyes heterophyes VON SIEBOLD <i>Coenogonimus heterophyes</i> , <i>Cotylagonimus heterophyes</i> , <i>Distomum heterophyes</i> , <i>Mesogonimus heterophyes</i>	Dimensions up to 2.7 x 0.9 mm.	1st intermediate host: water snails (in Egypt <i>Poronella conica</i>); 2nd intermediate host: mullet (<i>Mugil cephalus</i> syn. <i>Mugil japonicus</i>). Final host: cats, dogs and, where raw fish is eaten, man.	Very common in Egypt, Israel and the Far East. Otherwise as above (249).	As above (249). For bibliography see ¹ and ² .
174	251	Heterophyes katsuradai OSAKI ET ASADA	Dimensions ca. 0.75 x 0.5 mm.	?	As above (249).	As above (249).
174	252	Centrocestus armatus LOOSS <i>Stamnosoma armatum</i> TANABE	?	Intermediate host: fish. Final host: man (inter alia).	As above (249).	As above (249).
174	253	Echinostomum ilocanum GARRISON <i>Euparyphium ilocanum</i> , <i>Fasciolletta ilocana</i>	Length 2.5-10 mm, breadth 0.5-1.5 mm.	1st intermediate host: snails (<i>Gyranlus prashadi</i>). 2nd intermediate host: snails (<i>Pila luzonica</i>). Final host: rats and, where raw snails are eaten, man.	Intestinal parasite. Common in the Philippines.	As above (249). On <i>E. ilocanum</i> see ³ .
174	254	Euparyphium jassyense LEON ET CIUREA <i>Euparyphium melio (melis)</i>	Dimensions ca. 6 x 1.2 mm.	Host: man.	Intestinal parasite. Europe (esp. Rumania), Asia, North America.	As above (249).
174	255	Euparyphium malayanum LEIPER <i>Echinostoma malayanum</i>	Length 5-10 mm, breadth 2-3.5 mm.	Host: man.	Intestinal parasite. Malaya, Sumatra, Chinese-Tibetan border.	As above (249).
175	256	Schistosoma haematobium BILHARZ <i>Bilharzia haematobia</i> , <i>Bilharzia magna</i> , <i>Distomum capense</i> , <i>Gynaecophorus haematobius</i>	Males: length 8 to 16 mm, thickness 0.5 mm, with ventral groove (gynaecophoric canal) in which the female is taken up. In some species the mature female remains permanently in this groove.-Eggs 115-170 x 45-65 µm.	Intermediate host: snails (<i>Physopsis africana</i> , <i>P. globosa</i> , in Egypt mainly <i>Bullinus truncatus</i>). The forked-tail cercariae leave the snails, swim freely in water and penetrate the skin. Host: man.	Bilharziasis (schistosomiasis): the schistosomes live in the mesenteric and pelvic veins. The female deposits her eggs in the small vessels, whence they penetrate gradually into the intestine and bladder and pass out with the faeces and urine. <i>Sch. haematobium</i> causes above all inflammation of the urogenital system, bloody urine (papilloma formation), fistula and malignant tumours. Additionally splenomegaly, anaemia, ascites, liver-, heart- and lung-affectations.-Africa (above all Egypt, in ca. 60-85% of the population), Madagascar and south-west Asia.	Antimonials, e.g. tartar emetic.-Tetracyclins showed good results in the first tests. On schistosomiasis see ⁴ and ⁵ .
175	257	Schistosoma japonicum KATSURADA <i>Schistosoma cattoi</i>	Males 12-20 mm, females up to 26 mm. Eggs 70-100 x 50-65 µm.	Intermediate host: snails: <i>Amnicolidae</i> (<i>Katayama</i> , <i>Oncomelania</i> , <i>Schistosomophora</i>). Host: man.	As above (256). Orient inc. Japan, Philippines, Formosa, and parts of China.	As above (256).
175	258	Schistosoma mansoni SAMBON	Eggs as for <i>Sch. haematobium</i> (256).	Intermediate host: Planorbis snails (North Africa <i>Planorbis boissyi</i> , South Africa <i>Planorbis pfeifferi</i> , tropical America <i>Australorbis glabratus</i> = <i>Planorbis guadelupensis</i>). Host: man.	As above (256). Africa and tropical America, in Venezuela up to 90% of the male population over 10 years of age.-With <i>Sch. mansoni</i> the eggs are discharged only in the faeces so that symptoms in the urogenital tract are rarer than with <i>Sch. haematobium</i> .	As above (256).

¹) AFRICA, C., *Philipp. J. Sci.*, **57**, 253, 1935. ²) AFRICA et al., *Acta med. philipp.*, *Monogr. Ser.* **1**, 1940. ³) TUBANGUI, M. A., *Philipp. J. Sci.*, **51**, 581, 1933. ⁴) GIRGES, R., *Schistosomiasis*, London, 1934. ⁵) SCOTT, J. A., *Amer. J. Hyg.*, **25**, 566, 1937.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks Antibiotics Chemotherapeutics
		Platyhelminthes - continued				
176	259	Gastrodiscoides hominis LEWIS et MACCONNELL <i>Amphystomum hominis</i>	Length 4-8 mm, breadth 3-4 mm.	Nothing is known of the life-cycle. Normal host is apparently the pig.	Widespread in India, particularly in Assam (up to 40% of the population), Cochin China. Infests the coecum and large intestine and causes diarrhoea.	Chenopodium oil, santonin, carbon tetrachloride, etc. Soap-suds enema. On <i>G. hominis</i> see ¹ .
178	260	Diphyllbothrium latum LINNAEUS <i>Bothriocephalus latissimus</i> , <i>Bothriocephalus taenoides</i> , broad tapeworm, <i>Dibothriocephalus latus</i> , <i>Dibothrium latum</i> , fish tapeworm, ténia à épine	Length 2-10 m, breadth 10-12 up to 20 mm, segments broader than long, terminal segments almost square.	1st intermediate host: lower crustacea (Diaptoma). 2nd intermediate host: fish (species according to country). Final host: man, carnivores such as dogs, bears, etc.	World-wide distribution, in some areas, e.g. East Prussia, up to 100% of the population. - Infests the small intestine. - Symptoms: abdominal pains, loss of weight, progressive weakness. Causes severe pernicious anaemia with erythrocyte count down to 1 million. The incidence of anaemia appears to be race-dependent but is generally low; in Finland, for example, where proneness to anaemia is particularly marked, its incidence is only 1-2 in 10,000 infestations.	For tapeworm remedies, see footnote. For anaemia, liver extracts, vitamin B ₁₂ or folic acid SF. On <i>D. latum</i> see ² and ³ .
178	261	Sparganum mansonii	Plerocercoids of tapeworms of genus <i>Diphyllbothrium</i> (subgenus <i>Spirometra</i> , very probably <i>D. mansonii</i> and <i>D. erinacei</i>). Length 7.5-35 cm.	1st intermediate host of <i>Spirometra</i> group: lower crustacea (cyclops). 2nd intermediate host: amphibia, or warm-blooded animals which have consumed infested amphibia, also man. Final host: dogs, cats, possibly others.	<i>Sparganum</i> infestations are world-wide but mainly in Indochina, China and Japan. - In the East infestation also occurs by contact: native habit of applying split fresh frogs to inflammations and wounds. - <i>Sparganum</i> infests human muscle, subcutaneous connective tissue, or around the eye.	On <i>Sparganum mansonii</i> see ⁴ and ⁵ .
183	262	Dipylidium caninum LINNAEUS <i>Dipylidium cucumerinum</i> , <i>Taenia cucumerina</i> , <i>Taenia elliptica</i>	Length 1-4 m, breadth up to 3 mm, mature proglottids reddish colour.	Intermediate host: mallophaga (<i>Trichodectes canis</i>), dog-fleas (<i>Ctenocephalis canis</i>), also human fleas. Final host: dogs, cats, foxes, man.	Infestation by ingestion of infected dog-fleas or mallophaga. Human infestation is rare, mostly in children. - Infests small intestine.	For tapeworm remedies, see footnote. On <i>D. caninum</i> see ⁶ and ⁷ .
185	263	Hymenolepis nana VON SIEBOLD Dwarf tapeworm, <i>Taenia aegyptica</i> , <i>Taenia nana</i>	Length depends on the number of worms in the intestine, usually 20-30 mm, breadth 500-600 µm.	Normal host, in which the whole life-cycle takes place, is apparently man, but also infests rodents.	World-wide distribution, rarer in Europe, in North America up to 1-2% of the population, esp. children, in India up to 28% of the population.	See footnote: tapeworm remedies.

Tapeworm remedies (teniacides)

No absolutely certain remedy for tapeworms has yet been found. *Pumpkin seeds* are an old but nevertheless reliable and harmless remedy for children and are also useful for preliminary treatment of adults. Equally harmless and quite effective are *tin salts* (SnO and SnCl₂) and *purified light petroleum*. A further non-toxic remedy (except for a certain corrosive and anaesthetizing effect on the mucous membrane of the mouth) is *hexylresorcinol*. *Extract of male fern* is quite effective but unfortunately variable and toxic. Many other tapeworm remedies have been and still are recommended, such as carbon tetrachloride, quinacrine, etc.

According to WIGAND⁸ tin preparations and purified petroleum are usually effective. On the day before treatment very little food, purgatives, e.g. Carlsbad salt (no Epsom salts!). Last meal on previous evening, smoked or salted herrings, onions, raw carrots, garlic, also pumpkin seeds, etc.; absolute rest, also on the day of treatment. On the day of treatment itself preferably only tea, after the treatment saline purge again (cave MgSO₄!). Tin salts, hexylresorcinol, male-fern extract, orally; petroleum with duodenal tube.

NIMET BIYAL⁹ recommends the following dosage for **light petroleum (Petroleum Benzin U.S.P.)**:

Adults	60 ml
Children 2- 5 years	20 ml
6-14 years	30 ml

The petroleum is emulsified with acacia and a few drops of oil of peppermint added. The emulsion is warmed in hot water before use (N.B. highly inflammable!). It is contra-indicated in the presence of intestinal complaints. About 15% of failures have been reported.

TERADA and SAI¹⁰ recommend as a very effective teniacide *raigan*, a Chinese preparation of dried mushrooms (*Omphalia lapidescens*). Dose 3 × 1.25 g (20 grains) per day for three days.

If the scolex cannot be found in the stool after the treatment, then the latter should only be considered as having failed if tapeworm segments or eggs are again observed after ca. 12 weeks.

¹) BUCKLEY, J. J., *J. Helminth.*, **17**, 1, 1939. ²) VOGEL, M., *Z. Parasitenk.*, **2**, 213, 629, 1929-30. ³) CHANDLER, A. C., *Parasitology*, p. 312, 7th ed., New York, 1946. ⁴) BONNE, C., *Amer. J. trop. Med.*, **22**, 643, 1942. ⁵) IWATA, S., *Jap. J. Zool.*, **5**, 209, 1933. ⁶) ZIMMERMANN, H. R., *Z. Parasitenk.*, **9**, 717, 1937. ⁷) VERNARD, C. E., *Ann. N. Y. Acad. Sci.*, **37**, 273, 1938. ⁸) WIGAND, R., *Medizinische*, **2**, 1091, 1953. ⁹) NIMET BIYAL, *Schweiz. med. Wschr.*, **78**, 571, 1948. ¹⁰) TERADA and SAI, *Mansyu Igaku Zasshi (J. orient. Med.)*, **28**, 91, 1938.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks Antibiotics Chemotherapeutics
186	264	Platyhelminthes - continued Taenia solium LINNAEUS Armed tapeworm, Einsiedler-bandwurm, measly tapeworm, pork tapeworm, ver solitaire	Length 2-3 m, proglottids 1 m behind the head, square; mature segments 10-12 mm long, 5-6 mm wide.	Host: man (adult worms). Intermediate host: swine and man (bladder-worms). The oncospheres liberated from an egg ingested by the intermediate host (swine, but also man) enter the muscles and there develop into bladder-worms (<i>Cysticercus cellulosae</i>). Infestation occurs from ingestion of the cysticerci, which develop into adult tapeworms in the intestine. Man can also become infested through ingestion of the eggs, which develop into cysticerci in the muscles. It is also possible for cysticerci to arise from proglottids regurgitated from the stomach.	Abdominal pains, excessive appetite, weakness and loss of weight are the most usual symptoms. In general the pathogenicity is over-estimated, and the majority of <i>T. solium</i> and <i>T. saginata</i> infestations remain asymptomatic. - Infestation occurs mainly where pork is eaten, above all in Europe. It is remarkable that <i>T. solium</i> is rare in North America, the Philippines and India in spite of widespread consumption of pork. - Human beings carrying the tapeworm often carry also the bladder-worms. Localization occurs in all organs, esp. base of the brain, where ramified growth sometimes occurs (<i>Cysticercus ramosus</i>).	For tapeworm remedies see footnote on previous page. On <i>Cysticercus cellulosae</i> see ¹ and ² .
186	265	Taenia saginata GOEZE Beef tapeworm, fat tapeworm, <i>Taenia mediocanellata</i> , <i>Taeniorhynchus saginatus</i> , unarmed tapeworm	Length 4-10 m, mature segments in the form of pumpkin seeds, 16-20 mm long, 4-7 mm wide.	Host: man (adult worms). Intermediate host: cattle (cysticerci). Cysticerci (see above 264) in cattle (<i>Cysticercus bovis</i> , <i>Cysticercus inermis</i>). Development as for 264.	Pathogenicity as for <i>T. solium</i> (264). The commonest large tapeworm, distribution worldwide. In Africa, Tibet and Syria infests 25-75% of the population. Very rare in India (Hindu religion forbids eating of beef). - Cysticerci of <i>T. saginata</i> are very rarely observed in man.	For tapeworm remedies see footnote on previous page. <i>T. saginata</i> is more difficult to eradicate than <i>T. solium</i> . On <i>T. saginata</i> see ³ .
186	266	Echinococcus granulosus GOEZE Dog tapeworm, <i>Echinococcifer echinococcus</i> , hydatid tapeworm, <i>Taenia echinococcus</i>	Only 3 segments: total length 3-8 mm.	Host (adult worms): dogs, wolves, coyotes and related species. Often in thousands in the intestine. Intermediate host (larvae): practically all warm-blooded animals, esp. herbivores. The larvae of <i>Echinococcus granulosus</i> are known as echinococci (<i>Echinococcus polymorphus</i>).	Echinococci are found in all organs of the intermediate hosts. Daughter cysts may develop in the echinococcus cyst. When these swim freely in the mother cyst the whole is known as a hydatid cyst. These cause a characteristic noise on movement, due to rubbing of the daughter cysts. - Echinococci rarely form hydatid cysts in animals but they are frequent in man. - In sheep, swine and cattle (particularly in the liver) <i>Echinococcus multilocularis</i> or <i>alveolaris</i> is found, with cysts hardly the size of peas and held together by strands of tissue. Some authors consider this echinococcus to be the larva of a particular variety of tapeworm. <i>E. alveolaris</i> also occurs in man, nearly always in the liver, mainly in southern Europe and Asia. - <i>E. granulosus</i> is distributed over the whole world.	Surgical removal when possible. On echinococci in man, see ⁴⁻⁶ .

¹) BRAILSFORD, J., *Brit. J. Radiol.*, **14**, 79, 1941. ²) DIXON and SMITHERS, *Quart. J. Med.*, **45**, 1, 1935. ³) PENFOLD et al., *J. Helminth.*, **15**, 41, 1937. ⁴) DEW, H. R., *Hydatid Disease*, Sydney, 1928. ⁵) LOUCKS, H. H., *Nat. med. J. China*, **16**, 402, 1930. ⁶) MAGATH, T. B., *Amer. J. Hyg.*, **25**, 107, 1937.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks Antibiotics Chemotherapeutics
187	267	Nemathelminthes Strongyloides stercoralis BAVAY <i>Anguillula stercoralis</i> or <i>intestinalis</i> , <i>Rhabdonema intestinale</i> , <i>Rhabdonema stercorale</i> , <i>Rhabdonema strongyloides</i>	Parasitic form: length 2.6 mm, thickness 0.03 mm; free-living generation: ♂ 0.7 mm, ♀ 1 mm long.	Host: man. The larvae burrow into the skin and reach the right heart, lungs, bronchia, trachea via the veins, eventually migrating further into the pharynx and thence into the stomach and intestine, where the parasitic generation develops. The eggs of this form are passed with the faeces and develop into the free-living generation.	The penetration of the skin by the larvae often causes reddening of the skin and intense pruritus. Invasion of the lungs can cause acute pneumonia. The adult parasitic worms burrow deep into the intestinal mucosa. Mild infestation remains asymptomatic. In medium severe and chronic cases there is intermittent diarrhoea and epigastric pains. In severe cases uncontrollable diarrhoea (often bloody) with passing of undigested food particles and extreme water loss. Eosinophilia, leucocytosis, anaemia, slight fever, oedema are further intestinal symptoms.	Crystal violet (gentian violet). On <i>Strongyloides</i> see ¹ .
188	268	Wuchereria bancrofti COBBOLD <i>Filaria bancrofti</i> , <i>Filaria nocturna</i> , <i>Filaria philippinensis</i> , <i>Filaria sanguinis hominis</i> , <i>Wuchereria bancrofti</i>	Females 65-100 mm long, 0.25 mm thick, males half as long.	Host: man. Transmission by mosquitoes; in most countries: <i>Culex quinquefasciatus</i> ; Java: <i>Anopheles ludlovi</i> and <i>A. subpictus</i> ; Africa: <i>A. gambiae</i> ; China and Egypt: <i>Culex pipiens</i> ; Oceania: <i>Aedes scutellaris</i> ; the mosquitoes act only as intermediate hosts and passive carriers: when a warm-blooded animal is bitten the larvae break free from the labium, penetrate the skin of the victim and thus reach the blood stream. The sexually mature worms live in the lymph glands or ducts, often in inextricable tangles. See remarks.	Filariasis: the symptoms are due to obstruction of the lymphatic circulation and also partly to allergy. The symptoms appear very slowly, often 10-15 years after the first infection. The commonest manifestation of filariasis is elephantiasis (due to lymphatic obstruction and diversion) of various parts of the body, mainly the legs and scrotum, more rarely the arms, labia, breasts and parts of the head and neck.—Mainly prevalent in humid coastal areas and valleys of south-east Asia, East Indies, the Pacific islands, large parts of Africa, Queensland, West Indies, tropical America. The adult filaria copulate, whereupon the females give birth to microfilaria which are very mobile and appear periodically in the peripheral blood vessels. According to this periodicity the following are distinguished: <i>Microfilaria nocturna</i> , <i>diurna</i> and <i>perstans</i> . The microfilaria of <i>W. bancrofti</i> is a <i>nocturna</i> , that of <i>Loa loa</i> (see 270) a <i>diurna</i> . On filariasis and <i>W. bancrofti</i> , see ³⁻⁷ .	Hetrazan (trade name) = 1-diethylcarbamyl-4-methylpiperazine hydrochloride ^{2, 5} .
188	269	Wuchereria malayi (BRUG) RAO et MAPLESTONE BRUG's filaria	As for <i>W. bancrofti</i> (268).	Host: man. Transmission by mosquitoes of genus <i>Mansonia</i> , mainly <i>M. annulifera</i> (India) and <i>M. longipalpis</i> (Malaya).	Pathogenicity as for <i>W. bancrofti</i> . Elephantiasis mainly in the legs, rare in the scrotum.—Widely distributed in India (esp. Travancore, Madras, Bihar, Assam), south-east Asia and East Indies.	Hetrazan, see remarks on 268. On <i>W. malayi</i> see ⁸ and ⁹ .

¹) FAUST, E. C., *J. Amer. med. Ass.*, **98**, 2276, 1932. ²) *J. Amer. med. Ass.*, **150**, 625, 1952. ³) FULLEMANN, F., *Filariosen des Menschen, Handb. d. path. Mikroorganismen*, **6**, No. 28, 1093, 1931. ⁴) NAPIER, L. A., *Medicine*, **23**, 149, 1944. ⁵) KESSEL et al., *Amer. J. trop. Med. Hyg.*, **2**, 1050, 1953. ⁶) HAWKING, F., *Trans. roy. Soc. trop. Med. Hyg.*, **44**, 153, 1951. ⁷) BEYE et al., *Amer. J. trop. Med. Hyg.*, **1**, 637, 1952. ⁸) HODGKIN, E. P., *J. Malaya Branch Brit. med. Ass.*, **3**, 9, 1939. ⁹) RAO and MAPLESTONE, *Indian med. Gaz.*, **75**, 159, 1940.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name Synonyms	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks Antibiotics Chemotherapeutics
188	270	Nemathelminthes - continued Loa loa GUYOT African eye worm, <i>Dracunculus loa</i> , <i>Dracunculus oculi</i> , <i>Filaria bourgi</i> , <i>Filaria diurna</i> , <i>Filaria loa</i> , <i>Filaria oculi</i> , <i>Filaria sanguinis hominis maior</i>	Females 20-70 mm, males 30-35 mm long; resemble catgut.	Host: man. Transmitted by mango flies (<i>Chrysops dimidiata</i> , <i>C. silacea</i> , possibly others). Cf. also <i>W. bancrofti</i> (268).	Lives mainly in and around the eye, otherwise in the subcutaneous connective tissue. The worms are very mobile and wander from place to place under the skin at a speed of up to 1 inch in 2 minutes. The movement causes severe pruritus and unpleasant creeping sensations and is provoked or augmented by warmth (e.g. from a fire). <i>Loa loa</i> causes relatively little damage; infections are usually accompanied by painless oedematous swellings of the size of a pigeon's egg (Calabar swellings) which disappear after several days to reappear somewhere else. Worms in the eye can be easily extracted surgically, but the extraction must be expeditious before the disturbed worm flees to deeper places.	Hetrazan (see remarks on 268), but ineffective against the microfilaria ⁷ .
188	271	Onchocerca volvulus LEUCKART <i>Filaria volvulus</i>	Males 40 mm long × 0.2 mm thick. Females so long and tangled that entire specimens are difficult to get, but certainly 400 mm × 0.3 mm thick.	Host: man. The filaria from the female living in man penetrate the subcutaneous tissue as far as the skin and there gather under it in large numbers. Transmission by flies of the genus <i>Simulium</i> which serve as intermediate host (<i>S. damnosum</i> and <i>S. neavi</i> in Africa, <i>S. metallicum</i> , <i>S. ochraceum</i> , <i>S. callidum</i> , etc. in Guatemala and Mexico).	Causes swellings in the subcutaneous connective tissues up to the size of a pigeon's egg, growing at the rate of ca. 1 cm per year. Multiple swellings up to 200 often occur.-In central Africa, the mountains of Guatemala and south-west Mexico, mainly in the coffee regions.	Surgical removal. Hetrazan (see remarks on 268) is useless against the microfilaria ⁷ . On <i>Onchocerca</i> see ¹⁻⁴ .
188	272	Dracunculus medinensis VELSCHIUS Dragonneau, <i>Filaria aethiopica</i> , <i>Filaria medinensis</i> , guinea worm, Medina worm	Females 40-90 cm long; 0.5-1.7 mm thick. Males about the same size.	Host: man. Intermediate host and transmitter: lower crustacea (cyclops). The worm lives in the subcutaneous connective tissue and causes ulcers to form under the skin up to the size of a pigeon's egg. On breaking, the end of the mature worm is seen to protrude from the centre. On douching with cold water the larvae are ejected, each successive douching causing a further ejection. Eventually some of the larvae find and penetrate the crustacea, infestation arising when these are ingested.	The first symptoms appear with the formation of the ulcers and seem to be anaphylactic. They consist of urticaria, nausea, vomiting, diarrhoea, asthma, fainting. Later symptoms arise from bacterial infection of the ulcer. Marked eosinophilia.-Widely distributed from central India to Arabia, occasionally in East Indies, Egypt, and central Africa. Associated with dry climate, where cyclops is concentrated in localized water supplies with which the population come into contact (cf. life-cycle in left-hand column).	An old method still widely used is the gradual extraction of the worm by winding out on a stick, etc. Prior injections near the worm of phenothiazine (total 2-4 g) ease the extraction after 5-7 days. On <i>Dracunculus</i> see ⁵ . On phenothiazine injection see ⁶ .

¹) DAMPE, A., *Bol. Ofic. sanit. panamer.*, **21**, 753, 1942. ²) ORTLEPP, R. J., *J. S. Afr. vet. med. Ass.*, **8**, 1, 1937. ³) STRONG et al., *Amer. J. trop. Med.*, **18**, Suppl. 1, 1938. ⁴) STRONG et al., *Onchocercosis*, 1934. ⁵) FAIRLEY and LISTON, *Studies on Guinea Worm Disease*, Coll. papers from *Indian J. med. Res.*, *Indian med. Gaz.*, 1925. ⁶) ELLIOTT, W., *Trans. roy. Soc. trop. Med. Hyg.*, **35**, 291, 1942. ⁷) MADDEL and SPINGARN, *Amer. J. Med.*, **15**, 272, 1953.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks Antibiotics Chemotherapeutics
		Nemathelminthes - continued				
190	273	Trichuris trichiura LINNAEUS <i>Ascaris trichiura</i> , Haarschopf, <i>Trichocephalus crenatus</i> , <i>Trichocephalus dispar</i> , <i>Trichocephalus suis</i> , <i>Trichocephalus trichiurus</i> , whipworm	Length 30-50 mm, males have end of body curled up.	Very widespread in man and swine, appendix, small intestine. Infestation through water contaminated with the eggs, and from soil (dirty hands!).	Symptoms mostly not severe: abdominal pains as with appendicitis, indigestion, loss of appetite, loss of weight, etc. Heavy infestations cause severe diarrhoea and anaemia.	Tetracyclins gave good results in the first tests.- <i>Trichuris</i> is very difficult to expel: too far down the intestine to be reached in adequate concentration by anthelmintics and too far up to be reached by enemas. Most anthelmintics expel a few worms and the best appears to be hexylresorcinol. On <i>Trichuris</i> see ¹ .
190	274	Trichinella spiralis OWEN <i>Pseudalius trichina</i> , <i>Trichina spiralis</i> , trichina worm	Males 1.5 mm long, 0.04 mm thick; females 3-4 mm long, 0.06 mm thick.	The embryos produced by the trichina living in the intestine of the host migrate partly actively, partly passively into lymph or blood vessels throughout the body and finally enter striated muscles. Here they mature and roll themselves into spirals. The surrounding tissue degenerates and forms cysts round the worms. The cysts eventually become calcified. Infection through eating raw or insufficiently cooked meat. Host: apart from man, rats (normal host), swine, bears, dogs, etc. - World-wide distribution.	The intestinal trichina developing from ingested muscle trichina cause intestinal inflammation with diarrhoea and fever (typhous form). Migration into the muscles is accompanied by pains in the joints and increase in temperature (rheumatic form). The tendon reflex is absent and the respiration weak. Capillary haemorrhages in the eyes, oedema of the eyelids and in the knuckles. Eosinophilia, hyperleucocytosis (ca. 1-3 weeks after infection).-Experimentally (mice) the first infection leads to marked immunization.	Only treatment in the intestinal stage has any chance of success. The tetracyclins were effective in the first tests. On diagnosis of trichina infections, see ² .
197	275	Ancylostoma duodenale DUBINI <i>Dochmius duodenalis</i> , hookworm, <i>Uncinaria duodenalis</i>	Males 10 mm long, 0.5 mm thick; females 12-15 mm long.	The larvae in soil and water penetrate the skin, enter the blood stream, and thus reach the heart and lungs, whence they get into the trachea, pharynx, stomach and small intestine. Here they develop into mature worms.-World-wide distribution.	The worm lives in the small intestine of man, buried deep in the mucosa, and feeds by sucking blood. The consequent loss of blood causes severe anaemia with erythrocyte count down to 2 million per cu. mm and less.-Symptoms: <i>pre-intestinal phase</i> : the penetration of the skin by the larvae causes pruritus or inflammation ("ground itch", "water sore") also secondary bacterial infection (esp. with <i>Necator</i> , see 277). The migration in the body can cause pneumonia, leads to eosinophilia and occasionally to leucocytosis. <i>Intestinal phase</i> : several weeks after infestation anaemia develops, coupled with sluggishness, muscular weakness, rapid loss of breath on exertion, oedema, enlargement of the heart and palpitations, flatulence, abdominal disturbances. Capricious appetite, often a craving for "scratchy" substances such as soil, chalk and wood. - In children physical and mental retardation, the latter resulting in backwardness at school. - The results in pregnancy are especially severe, more so than with syphilis or eclampsia, and cause a large number of stillbirths.	Tetrachlorethylene is the preferred remedy, carbon tetrachloride being equally effective but more toxic. The anaemia should be treated with iron (in case of diarrhoea, parenteral administration). It is remarkable that for an unknown reason iron therapy causes the worms to disappear rapidly. On hookworm see ³⁻⁵ .
197	276	Ancylostoma braziliense G. DE FARIA	Somewhat smaller than <i>A. duodenale</i> .	As above (275).	As above (275).	As above (275).
198	277	Necator americanus W. STILES American hookworm, <i>Ancylostoma americanum</i> , <i>Necator argentinus</i> , <i>Uncinaria americana</i>	Somewhat smaller than <i>A. duodenale</i> , but very similar and often mistaken for it.	As above (275).	As above (275).	As above (275).

¹) SWARTZWELDER, J. C., *Amer. J. trop. Med.*, **19**, 473, 1938. ²) *J. Amer. med. Ass.*, **104**, 1801, 1935. ³) ANDREWS, J., *Amer. J. publ. Hlth*, **32**, 382, 1942. ⁴) CHANDLER, A. C., *Hookworm Disease*, New York, 1929. ⁵) FOSTER and LANDSBERG, *Amer. J. Hyg.*, **20**, 259, 1934. ⁶) KELLER et al., *Amer. J. trop. Med.*, **20**, 493, 1940. ⁷) LANE, C., *Hookworm Infection*, London, 1932. ⁸) MAPLESTONE and MUKERJI, *Indian med. Gaz.*, **72**, 650, 1937.

For bibliography and legend, see page 129

See pages 169-171	See pages 172-178	Name <i>Synonyms</i>	Principal characteristics	Habitat, host, transmission, etc.	Diseases	Remarks Antibiotics Chemotherapeutics
202	278	Nemathelminthes - concluded Ascaris lumbricoides LINNAEUS <i>Ascaris ovis</i> , <i>Ascaris suilla</i> , eel-worm, roundworm, Spulwurm, ver lombricoide	Males 150-170 mm long, 3 mm thick; females 200-250 mm long, 5 mm thick.	Host: frequent in small intestine of man, swine, occasionally dogs, cattle. Infestation arises from raw vegetables contaminated with the eggs (liquid manuring!). Self-infection is impossible since eggs passed in faeces must have laid 30-40 days in the open (summer) before the embryos develop. <i>Ascaris</i> eggs remain infective 5-7 years in soil, as shown experimentally ¹³ . - Distribution world-wide.	The embryos produced from eggs in the stomach reach the pharynx via the blood stream, heart, lungs and trachea, and thence enter the small intestine. The migration can cause pneumonia and always results in eosinophilia. - Symptoms depend on the severity of the infestation. - Since the worms show a marked inclination to wander they can reach the bile duct, more rarely the pancreatic duct, and cause obstruction. - Occasionally they break through the intestinal wall and cause peritonitis. - Cases with 1000-5000 worms have been described. In such quantities they can completely block the intestine and must be removed surgically.	Hexylresorcinol; chenopodium oil and santonin are somewhat more toxic but equally effective.
205	279	Enterobius vermicularis LINNAEUS <i>Fusarella vermicularis</i> , <i>Oxyuris vermicularis</i> , pinworm, Pfric-menschwanz, seatworm	Males 2-5 mm, females 8-13 mm long.	Host: man. The eggs are deposited in the peri-anal region and reach the mouth by self-infection (finger nails, etc.). - Distribution world-wide: the number of human beings infected is estimated at 209 millions in the whole world ⁷ , the percentage varying between 1% (Guam ⁸), 32% (Texas ⁹), 60% (Canada ¹⁰) and 85 to 100% (Amsterdam ^{11,12}).	The nightly emigrations of the worms from the anus for the purpose of egg-laying cause severe pruritus which leads to scratching and thus continuous reinfection via the mouth. - The adult worms live in the caecum, appendix and neighbouring regions. The males remain there and die shortly after copulation while the females wander into the rectum to lay their eggs. In isolated cases they also infest the vagina.	Of about equal efficacy are crystal violet (gentian violet) (82%) and the tetracyclins (84%) ¹ . Strict personal and family hygiene! The whole family should always be treated. Tetracyclins hinder the ripening of the eggs and lead to the laying of unripe eggs. Duration of treatment 7 to 10 days ² . On enterobiasis see ¹ and ³⁻⁵ . On diagnosis see ⁶ .
	280	Fungi Candida albicans ROBIN <i>Endomyces albicans</i> , <i>Monilia albicans</i> , <i>Mycotorula albicans</i> , <i>Oidium albicans</i> , <i>Parasaccharomyces harteri</i> , <i>Saccharomyces albicans</i> , <i>Syngospora robini</i> ; identical with: (<i>Blastodendron</i>) <i>B. erectum</i> , <i>B. faurei</i> , <i>B. intestinale</i> , <i>B. pinoyi</i> ; (<i>Candida</i>) <i>C. pinoyisimilis</i> ; (<i>Geotrichoides</i>) <i>G. krusei</i> , <i>G. tumefaciens</i> ; (<i>Mycotorula</i>) <i>M. actoni</i> , <i>M. alba</i> , <i>M. alvarezsotoi</i> , <i>M. armeniensis</i> , <i>M. bethaliensis</i> , <i>M. buccalis</i> , <i>M. decolorans</i> , <i>M. faecalis</i> , <i>M. glycopbila</i> , <i>M. harteri</i> , <i>M. inexorabilis</i> , <i>M. laryngitidis</i> , <i>M. mannitofermentans</i> , <i>M. metalondinensis</i> , <i>M. nabarroii</i> , <i>M. oosporoides</i> , <i>M. ovalis</i> , <i>M. periunguealis</i> , <i>M. pseudo-albicans</i> , <i>M. pseudo-londinensis</i> , <i>M. pseudo-londinoides</i> , <i>M. psilosis</i> , <i>M. quasilinguae-pilosae</i> , <i>M. rboi</i> , <i>M. richmondi</i> , <i>M. vaginalis</i> , <i>M. verticillata</i> ; (<i>Syngospora</i>) <i>S. negronii</i> ; (<i>Cryptococcus</i>) <i>C. copellii</i>	Forms white membranes on the mucosa, usually easily detached.	Saprophyte of man and many other warm-blooded animals, on mucosa of mouth, nose, pharynx, vagina, and other body cavities.	Cause of moniliasis (thrush, white mouth, oidiomycosis, moniliids, erosio interdigitalis). Facultatively pathogenic (in weakened subjects, esp. children), usually a harmless saprophyte. - In therapy with antibiotics there is a danger that the suppression of the normal bacterial flora may permit <i>C. albicans</i> to multiply unhindered (respiratory passages, lungs, intestinal tract). In debilitated children (esp. infants) it is therefore advisable to pay special attention to moniliasis when using broad-spectrum antibiotics (tetracyclins). If an infection already exists these antibiotics are contraindicated.	The methyl and propyl esters of <i>p</i> -hydroxybenzoic acid (methyl- and propyl-paraben) are best suited to the treatment of intestinal and local moniliasis. In the oral application of tetracyclins the simultaneous administration of vitamin-B complex appears to hinder the development of intestinal mycoses.

¹) BUMBALO et al., *Amer. J. Dis. Child.*, **86**, 592, 1953. ²) LOUGHLIN, H. E., *Antibiot. and Chemother.*, **1**, 588, 1951. ³) BRADY and WRIGHT, *Amer. J. med. Sci.*, **198**, 367, 1939. ⁴) CRAM, E. R., *Amer. J. Dis. Child.*, **65**, 46, 1943. ⁵) BRADY, F. J., *Amer. Pract.*, **1**, 583, 1947. ⁶) HALL, M. C., *Amer. J. trop. Med.*, **17**, 445, 1937. ⁷) STOLL, N. R., *J. Parasit.*, **33**, 1, 1947. ⁸) STOLL et al., *Puerto Rico J. publ. Hlth*, **22**, 235, 1947. ⁹) KILLINGSWORTH et al., *Texas J. Med.*, **48**, 27, 1952. ¹⁰) KUITUNEN-ECKBAUM, E., *Canad. med. Ass. J.*, **48**, 229, 1943. ¹¹) HUMMELEN, L. R., *Helminthiasis in Children*, Thesis, Amsterdam, 1945. ¹²) SCHÜFFNER, W., *Klin. Wschr.*, **22**, 521, 1944. ¹³) MÜLLER, G., *Zbl., Bakt., I. Abt. Ref.*, **159**, 377, 1953.

Bacteria

The ever-widening scope of bacteriological knowledge still precludes the setting up of a system of classification which can make any claim to finality. The systematic classification and nomenclature which follows on pages 169–171 has been taken from BREED, MURRAY and HITCHENS, *Bergey's Manual of Determinative Bacteriology*, 6th edition, Baltimore, 1948. For other systems, see LEHMANN and NEUMANN, *Bakt. Diag.*, 7th edition, Munich, 1927; WEINBERG, NATIVELLE and PRÉVOT, *Les microbes anaérobies*, Paris, 1937; PRIBRAM, *Klassifikation der Schizomyceten*, Leipzig and Vienna, 1933.

Nomenclature: In accordance with international convention groups higher than the family are designated by the suffix *-ales*, families by *-aceae*, subfamilies by *-oideae*, tribes by *-eae*, subtribes by *-inae*. In addition, the suffix *-ineae* is used in *Bergey's Manual* for suborders.

Only a minority of the families and genera listed in the following classification are pathogenic. It has been reproduced in its entirety in order to provide the interested reader with a complete picture. The figures after the names are reference numbers which enable the appropriate classifications of the pathogenic organisms listed in the tables "Pathogens, Infectious Diseases and Antibiotics" on pages 129–168 to be found (column 1, bold figures).

Protozoa and Worms

The systematic classification of protozoa and worms has been taken from FIEBIGER, J., *Die tierischen Parasiten*, 4th edition, Vienna, 1947; the nomenclature is based partly on BRUMPT, E., *Précis de Parasitologie*, 6th edition, Paris, 1949, and partly on CHANDLER, A. C., *Parasitology*, 7th edition, New York, 1946.

Class Schizomycetes NÄGELI

Order I. Eubacteriales BUCHANAN

Suborder I. Eubacteriineae BREED, MURRAY et HITCHENS

Family I. Nitrobacteriaceae BUCHANAN

Tribe I. Nitrobacterieae WINSLOW et al.		
Genus I.	<i>Nitrosomonas</i> WINOGRADSKY	1
Genus II.	<i>Nitrosococcus</i> WINOGRADSKY	2
Genus III.	<i>Nitrospira</i> WINOGRADSKY	3
Genus IV.	<i>Nitrosocystis</i> WINOGRADSKY	4
Genus V.	<i>Nitrosogloea</i> H. WINOGRADSKY	5
Genus VI.	<i>Nitrobacter</i> WINOGRADSKY	6
Genus VII.	<i>Nitrocystis</i> H. WINOGRADSKY	7

Tribe II. Hydrogenomonadeae PRIBRAM		
Genus I.	<i>Hydrogenomonas</i> ORLA-JENSEN	8

Tribe III. Thiobacilleae BERGEY, BREED et MURRAY		
Genus I.	<i>Thiobacillus</i> BEIJERINCK	9

Family II. Pseudomonadaceae WINSLOW et al.

Tribe I. Pseudomonadeae KLUYVER et VAN NIEL		
Genus I.	<i>Pseudomonas</i> MIGULA	10
Genus II.	<i>Xanthomonas</i> DOWSON	11
Genus III.	<i>Methanomonas</i> ORLA-JENSEN	12
Genus IV.	<i>Acetobacter</i> BEIJERINCK	13
Genus V.	<i>Protaminobacter</i> DEN DOOREN DE JONG	14
Genus VI.	<i>Mycoplana</i> GRAY et THORNTON	15

Tribe II. Spirilleae KLUYVER et VAN NIEL		
Genus I.	<i>Vibrio</i> MÜLLER	16
Genus II.	<i>Desulfovibrio</i> KLUYVER et VAN NIEL	17
Genus III.	<i>Cellvibrio</i> WINOGRADSKY	18
Genus IV.	<i>Cellfalcicula</i> WINOGRADSKY	19
Genus V.	<i>Thiospira</i> VISLOUCH	20
Genus VI.	<i>Spirillum</i> EHRENBERG	21

Family III. Azotobacteriaceae BERGEY, BREED et MURRAY		
Genus I.	<i>Azotobacter</i> BEIJERINCK	22
(classification uncertain:)		
Genus A.	<i>Azotomonas</i> STAPP	23

Family IV. Rhizobiaceae CONN		
Genus I.	<i>Rhizobium</i> FRANK	24
Genus II.	<i>Agrobacterium</i> CONN	25
Genus III.	<i>Chromobacterium</i> BERGONZINI	26

Family V. Micrococcaceae PRIBRAM		
Genus I.	<i>Micrococcus</i> COHN	27
(classification uncertain:)		
Genus A.	<i>Methanococcus</i> KLUYVER et VAN NIEL	28
Genus B.	<i>Pediococcus</i> BALCKE	29
Genus II.	<i>Gaffkya</i> TREVISAN	30
Genus III.	<i>Sarcina</i> GOODSIR	31

Family VI. Neisseriaceae PRÉVOT		
Genus I.	<i>Neisseria</i> TREVISAN	32
Genus II.	<i>Veillonella</i> PRÉVOT	33

Family VII. Lactobacteriaceae ORLA-JENSEN		
Tribe I. Streptococcaceae TREVISAN		
Genus I.	<i>Diplococcus</i> WEICHELBAUM	34
Genus II.	<i>Streptococcus</i> ROSENBAACH	35
Genus III.	<i>Leuconostoc</i> VAN TIEGHEM	36

Tribe II. Lactobacilleae WINSLOW et al.		
Genus I.	<i>Lactobacillus</i> BEIJERINCK	37
(classification uncertain:)		
Genus A.	<i>Leptotrichia</i> TREVISAN	38
Genus II.	<i>Microbacterium</i> ORLA-JENSEN	39
Genus III.	<i>Propionibacterium</i> ORLA-JENSEN	40
Genus IV.	<i>Butyribacterium</i> BARKER	41

Family VIII. Corynebacteriaceae LEHMANN et NEUMANN		
Genus I.	<i>Corynebacterium</i> LEHMANN et NEUMANN	42
Genus II.	<i>Listeria</i> PIRIE	43
Genus III.	<i>Erysipelothrix</i> ROSENBAACH	44

Family IX. Achromobacteriaceae		
Genus I.	<i>Alcaligenes</i> CASTELLANI et CHALMERS	45
Genus II.	<i>Achromobacter</i> BERGEY et al.	46
Genus III.	<i>Flavobacterium</i> BERGEY et al.	47

Family X. Enterobacteriaceae RAHN		
Tribe I. Eschericheae BERGEY, BREED et MURRAY		
Genus I.	<i>Escherichia</i> CASTELLANI et CHALMERS	48
Genus II.	<i>Aerobacter</i> BEIJERINCK	49
Genus III.	<i>Klebsiella</i> TREVISAN	50
(classification uncertain:)		
Genus A.	<i>Paracolobactrum</i> BORMAN, STUART et WHEELER	51

Tribe II. Erwineae WINSLOW et al.		
Genus I.	<i>Erwinia</i> WINSLOW et al.	52

Tribe III. Serrateae BERGEY, BREED et MURRAY		
Genus I.	<i>Serratia</i> BIZIO emend. BREED et BREED	53

Tribe IV. Proteae CASTELLANI et CHALMERS		
Genus I.	<i>Proteus</i> HAUSER	54

Tribe V. Salmonelleae BERGEY, BREED et MURRAY		
Genus I.	<i>Salmonella</i> LIGNIÈRES	55
Genus II.	<i>Shigella</i> CASTELLANI et CHALMERS	56

Family XI. Parvobacteriaceae RAHN		
Tribe I. Pasteurelleae CASTELLANI et CHALMERS		
Genus I.	<i>Pasteurella</i> TREVISAN	57
Genus II.	<i>Malleomyces</i> HALLER	58
Genus III.	<i>Actinobacillus</i> BRUMPT	59
(classification uncertain:)		
Genus A.	<i>Donovania</i> ANDERSON et al.	60

Schizomycetes (continued)

Order I. Eubacteriales (continued)

Suborder I. Eubacteriineae (continued)

Family XI. Parvobacteriaceae (continued)

Tribe II. <i>Brucelleae</i> BERGEY, BREED et MURRAY	
Genus I.	<i>Brucella</i> MEYER et SHAW 61
Tribe III. <i>Bacteroidae</i> BREED, MURRAY et HITCHENS	
Genus I.	<i>Bacteroides</i> CASTELLANI et CHALMERS 62
Genus II.	<i>Fusobacterium</i> KNORR 63
Tribe IV. <i>Haemophilae</i> WINSLOW et al.	
Genus I.	<i>Haemophilus</i> WINSLOW et al. 64
Genus II.	<i>Moraxella</i> LWOFF 65
Genus III.	<i>Noguchia</i> OLITSKY, SYVERTON et TYLER 66
Genus IV.	<i>Dialister</i> BERGEY et al. 67

Tribe <i>Mimeae</i> DE BORD 68	
------------------------------------------	--

Family XII. Bacteriaceae COHN

Genus I.	<i>Bacterium</i> EHRENBERG 70
----------	-----------------------------------------

Family XIII. Bacillaceae FISHER

Genus I.	<i>Bacillus</i> COHN 71
Genus II.	<i>Clostridium</i> PRAZMOWSKI 72

Suborder II. Canlobacteriineae BREED, MURRAY et HITCHENS

Family I. Nevskiaceae HENRICI et JOHNSON

Genus I.	<i>Nevskia</i> FAMINTZIN 73
----------	---------------------------------------

Family II. Gallionellaceae HENRICI et JOHNSON

Genus I.	<i>Gallionella</i> EHRENBERG 74
----------	-------------------------------------------

Family III. Canlobacteriaceae HENRICI et JOHNSON

Genus I.	<i>Canlobacter</i> HENRICI et JOHNSON 75
----------	----------------------------------------------------

Family IV. Siderocapsaceae PRIBRAM

Genus I.	<i>Siderocapsa</i> MOLISCH 76
Genus II.	<i>Sideromonas</i> CHOLODNY 77

Family (classification uncertain) Pasteuriaceae LAURENT

Genus I.	<i>Pasteuria</i> METCHNIKOFF 78
Genus II.	<i>Blastocaulis</i> HENRICI et JOHNSON 79

Suborder III. Rhodobacteriineae BREED, MURRAY et HITCHENS

Family I. Thiorhodaceae MOLISCH

Genus I.	<i>Thiosarcina</i> WINOGRADSKY 80
Genus II.	<i>Thiopedia</i> WINOGRADSKY 81
Genus III.	<i>Thiocapsa</i> WINOGRADSKY 82
Genus IV.	<i>Thiodictyon</i> WINOGRADSKY 83
Genus V.	<i>Thiothece</i> WINOGRADSKY 84
Genus VI.	<i>Thiocystis</i> WINOGRADSKY 85
Genus VII.	<i>Lamprocystis</i> SCHROETER 86
Genus VIII.	<i>Amoebobacter</i> WINOGRADSKY 87
Genus IX.	<i>Thioplycoccus</i> WINOGRADSKY 88
Genus X.	<i>Thiospirillum</i> WINOGRADSKY 89
Genus XI.	<i>Rhabdomonas</i> COHN 90
Genus XII.	<i>Rhodothece</i> MOLISCH 91
Genus XIII.	<i>Chromatium</i> PERTY 92

Family II. Athiorhodaceae MOLISCH

Genus I.	<i>Rhodopseudomonas</i> KLUYVER et VAN NIEL emend. VAN NIEL 93
Genus II.	<i>Rhodospirillum</i> MOLISCH 94

Family III. Chlorobacteriaceae GEITLER et PASCHER

Genus I.	<i>Chlorobium</i> NADSON 95
Genus II.	<i>Pelodictyon</i> LAUTERBORN 96
Genus III.	<i>Clathrochloris</i> GEITLER 97
Genus IV.	<i>Chlorobacterium</i> LAUTERBORN 98
Genus V.	<i>Chlorochromatium</i> LAUTERBORN 99
Genus VI.	<i>Cylindrogloea</i> PERFILIEW 100

Order II. Actinomycetales BUCHANAN

Family I. Mycobacteriaceae CHESTER

Genus I.	<i>Mycobacterium</i> LEHMANN et NEUMANN 101
----------	-------------------------------------------------------

Family II. Actinomycetaceae BUCHANAN

Genus I.	<i>Nocardia</i> TREVISAN 102
Genus II.	<i>Actinomyces</i> HARZ 103

Family III. Streptomycetaceae WAKSMAN et HENRICI

Genus I.	<i>Streptomyces</i> WAKSMAN et HENRICI 104
Genus II.	<i>Micromonospora</i> ØRSKOV 105

Order III. Chlamydobacteriales BUCHANAN

Family I. Chlamydobacteriaceae MIGULA

Genus I.	<i>Sphaerotilus</i> KÜTZING 106
Genus II.	<i>Clonothrix</i> ROZE 107
Genus III.	<i>Leptothrix</i> KÜTZING 108

Family II. Crenothricaceae HANSGIRG

Genus I.	<i>Crenothrix</i> COHN 109
----------	--------------------------------------

Family III. Beggiatoaceae MIGULA

Genus I.	<i>Thiothrix</i> WINOGRADSKY 110
Genus II.	<i>Beggiatoa</i> TREVISAN 111
Genus III.	<i>Thiospirillopsis</i> UPHOF 112
Genus IV.	<i>Thioploca</i> LAUTERBORN 113

Family (classification uncertain) Achromatiaceae MASSART

Genus I.	<i>Achromatium</i> SCHEWIAKOFF 114
Genus II.	<i>Thiovulum</i> HINZE 115
Genus III.	<i>Macromonas</i> UTERMÖHL et KOPPE 116

Order (classification uncertain) Caryophanales PESHKOFF

Family I. Pontothricaceae PESHKOFF

Genus I.	<i>Pontothrix</i> NADSON et KRASSILNIKOW 117
----------	--------------------------------------------------------

Family II. Arthromitaceae PESHKOFF

Genus I.	<i>Arthromitus</i> LEIDY 118
Genus II.	<i>Coleomitus</i> DUBOSCQ et GRASSÉ 119

Family III. Oscillospiraceae PESHKOFF

Genus I.	<i>Oscillospira</i> CHATTON et PERARD
----------	-------------------------------------------------

Family IV. Caryophanaceae PESHKOFF

Genus I.	<i>Caryophanon</i> PESHKOFF 120
----------	-------------------------------------------

Order IV. Myxobacteriales JAHN

Family I. Cytophagaceae STANIER

Genus I.	<i>Cytophaga</i> STANIER 121
----------	----------------------------------------

Family II. Archangiaceae JAHN

Genus I.	<i>Archangium</i> JAHN 122
Genus II.	<i>Stelangium</i> JAHN 123

Family III. Sorangiaceae JAHN

Genus I.	<i>Sorangium</i> JAHN 124
----------	-------------------------------------

Family IV. Polyangiaceae JAHN

Genus I.	<i>Polyangium</i> JAHN 125
Genus II.	<i>Synangium</i> JAHN 126
Genus III.	<i>Melittangium</i> JAHN 127
Genus IV.	<i>Podangium</i> JAHN 128
Genus V.	<i>Chondromyces</i> BERKELEY et CURTIS 129

Schizomycetes (continued)

Order IV. Myxobacterales (continued)

Family V. Myxococcaceae JAHN

Genus I.	<i>Myxococcus</i> THAXTER	130
Genus II.	<i>Chondrococcus</i> JAHN	131
Genus III.	<i>Angiococcus</i> JAHN	132
Genus IV.	<i>Sporocytophaga</i> STANIER	133

Order V. Spirochaetales BUCHANAN

Family I. Spirochaetaceae SWELLENGREBEL

Genus I.	<i>Spirochaeta</i> EHRENBERG	134
Genus II.	<i>Saprosira</i> GROSS	135
Genus III.	<i>Cristispira</i> GROSS	136

Family II. Treponemataceae SCHAUDINN

Genus I.	<i>Borrelia</i> SWELLENGREBEL	137
Genus II.	<i>Treponema</i> SWELLENGREBEL	138
Genus III.	<i>Leptospira</i> NOGUCHI	139

Order (classification uncertain) Rickettsiales GIESZCYKIEWICZ

Family I. Rickettsiaceae PINKERTON

Genus I.	<i>Rickettsia</i> DA ROCHA-LIMA	140
Genus II.	<i>Coxiella</i> BENGTON	141
Genus III.	<i>Cowdria</i> BENGTON	142

Family II. Bartonellaceae GIESZCYKIEWICZ

Genus I.	<i>Bartonella</i> STRONG, TYZZER et SELLARDS	143
Genus II.	<i>Haemobartonella</i> TYZZER et WEINMAN	144
Genus III.	<i>Grahamella</i> BRUMPT	145
Genus IV.	<i>Eperythrozoon</i> SCHILLING	146

Family III. Chlamydozoaceae MOSKOVSKY

Genus I.	<i>Chlamydozoon</i> HALBERSTAEDTER et VON PROWAZEK	147
Genus II.	<i>Miyagawanella</i> BRUMPT	148
Genus III.	<i>Colesiota</i> RAKE	149
(classification uncertain:)		
Genus A.	<i>Caryococcus</i> DANGEARD	150
Genus B.	<i>Drepanospira</i> PETSCHENKO	151
Genus C.	<i>Holospira</i> HAPKINE	152

Order (classification uncertain) Virales 153

Protozoa

A. Class: Rhizopoda (Sarcodina)

1. Order: Amoebina (Gymnamoebida)	154
---------------------------------------------	-----

B. Class: Mastigophora

Subclass: Flagellata

1. Order: Protomonadina

Family: Cercomonadidae	155
Family: Bodonidae	156
Family: Trypanosomidae	157

2. Order: Polymastigina

Family: Tetramitidae	158
Family: Distomatidae	159

C. Class: Sporozoa

Subclass: Telosporidia

1. Order: Coccidiaria

Family: Eimeridae	160
Family: Adelaidae	161

2. Order: Haemosporidia

Family: Plasmodidae	162
Family: Haemoproteidae	163
Family: Leucocytozoidae	164

Subclass: Cnidosporidia

1. Order: Microsporidia

Family: Nosematidae	165
-------------------------------	-----

2. Order: Myxosporidia

Family: Myxidiidae	166
Family: Chloromyxidae	167
Family: Myxobolidae	168

Subclass: Sarcosporidia

D. Class: Ciliata (Infusoria) 169

Vermes (Worms)

A. Class: Platyhelminthes (Flatworms, parenchymatous worms)

Subclass: Trematoda

1. Order: Monogenea

Family: Tristomidae	170
Family: Polystomidae	171
Family: Gyrodactylidae	172

2. Order: Digenea

Family: Monostomidae	173
Family: Fasciolidae	174
Family: Schistosomidae	175
Family: Paramphistomidae	176
Family: Strigeidae	177

Subclass: Cestoda (Tapeworms)

1. Order: Pseudophyllidea

Family: Diphyllbothriidae	178
-------------------------------------	-----

2. Order: Cyclophyllidea

Family: Mesocostoididae	179
Family: Anoplocephalidae	180
Family: Davaineidae	181
Family: Fimbriariidae	182
Family: Dipylidiidae	183
Family: Dilepididae	184
Family: Hymenolepididae	185
Family: Taeniidae	186

B. Class: Nematelminthes (Roundworms)

1. Order: Nematoda (Threadworms)

Superfamily: Rhabditoidea	187
Superfamily: Filarioidea	188
Superfamily: Spiruroidea	189
Superfamily: Trichuroidea	190
Superfamily: Dioctophymioidea	191
Superfamily: Strongyloidea	

Family: Metastrongylidae	192
Family: Trichostrongylidae	193

Family: Strongylidae

Subfamily: Oesophagostominae	194
Subfamily: Strongylinae	195
Subfamily: Trichoneminae	196
Subfamily: Ancylostominae	197
Subfamily: Necatorinae	198
Subfamily: Syngamminae	199
Subfamily: Stephanurinae	200

Superfamily: Ascaroidea

Family: Ascaridae	201
Subfamily: Ascarinae	202
Subfamily: Ascaridiinae	203
Subfamily: Anisakinae	204

Family: Oxyuridae

Subfamily: Oxyurinae	205
Subfamily: Heterakinae	206
Subfamily: Subulurinae	207

2. Order: Acanthocephali (Spiny-headed worms)

C. Class: Annelida (Segmented worms)

Subclass: Hirudinea (Leeches)

Index of Pathogenic Organisms (Bacteria, Protozoa, Worms) and Infectious Diseases

The *italic numbers* in this index are reference numbers corresponding to the *italic numbers* in column 2 of the tables on pages 129-168. Further information on any pathogenic organism (synonyms, characteristics, vectors, diseases, susceptibility to antibiotics, etc.) or infectious disease listed may therefore readily be found by looking under the appropriate number in column 2 of the tables.

A	
A-Encephalitis	195
Abortion, epidemic epizootic	89, 90
Ab-oukine, aboukoué	160
Abscesses	5, 25, 30, 36, 45, 53, 54, 92, 93, 219
Acne	49
— varioliformis	191
Actinobacillosis	86
Actinobacillus lignieresii	86
— mallei	85
Actinobacterium israeli	135
Actinomyces acnes	49
— africanus	137
— asteroides	130
— beddardii	144
— bifidus	47
— bovis	134
— bovis sulphureus	134
— eppingeri	130
— erysipeloidis	52
— fordii	136
— gallicus	138
— gibsonii	143
— hortonsensis	142
— indicus	132
— israeli	135
— kimberi	145
— leishmani	131
— listeri	140
— luteus	133
— madurae	132
— muris	100
— muris ratti	100
— pelletieri	139
— rosenbachii	52
— somaliensis	146
— sulphureus	134
— thuillieri	51
— upcottii	141
— willmorei	147
— wolff-israel	135
Actinomyces	86, 130-147
Acuformis alcaligenes	125
— innutritus	120
— macrosporus	122
Acystia typhi	72
Adrenal haemorrhage	16
Aerobacter aerogenes	55
— cloacae	56
— coli	54
African eye worm	270
Aki-yami	165-167
Alastrim	185
Albococcus epidermidis	9
— pyogenes	6
Alcaligenes abortus	89
— bronchisepticus	91
— faecalis	53
— melitensis	88
Aleppo boil	234
Alveolar infections	25, 26, 161, 221
Amoeba buccalis	221
— coli	219
— dentalis	221
— intestini vulgaris	220
— limax	222
Amoebiasis	219, 224
Amphistomum hominis	259
Amygdalitis (tonsillitis)	5, 10, 11, 33-35
Anaemia 246, 248, 256-258, 260, 267, 273, 275-277	
— equine infectious	213
Anaeromyces bronchitica	135
Ancylostoma americanum	277
— braziliense	276
— duodenale	275
Angina	34, 35
— LUDWIG'S	41
— PLAUT-VINCENT	94, 153
Anguillula intestinalis (stercoralis)	267
Anthrax	109
Aplanobacter anthracis	109
Appendicitis	33, 40-45, 92, 93, 279
Appendix, infections	36
Arthritis, purulent	5
Ascaris lumbricoides	278
— ovis	278
— suilla	278
— trichiura	273
Ascites	246, 256-258

A	
Asterococcus muris	100
Asteroides asteroides	130
Asthma	272
Atrophic paralysis	200
Aurococcus aurantiacus	8
— aureus	5
Aussatz (leprosy)	129
Azul	164
B	
B-Encephalitis	196
Babesia erysipeloides	52
Bacille A de WEINBERG et SEGUIN	110
— B de WEINBERG et SEGUIN	112
— D de WEINBERG et SEGUIN	114
— de MORAX	101
— de SONNE	81
— de la coqueluche	98
— de la morve	85
— pyocyanique	1
— du rouget	51
— tétanique	123
Bacillus, BIENSTOCK'S	124
— BOAS-OPPLER	46
— BORDET-GENGOU	98
— E. ADAMSON	119
— EBERTH'S	72
— FRIEDLAENDER'S	57
— GÄRTNER'S	73
— KLEBS-LOEFFLER	48
— PFEIFFER'S	95
— SCHMITZ'S	77
— tetanus	123
Bacillus abortus	89
— abortus-suis	90
— acidophilus	46
— acnes	49
— aerofoetidus	114
— aerogenes	55
— aerogenes capsulatus	117
— aertrycke	69
— aeruginosus	1
— albuminis	124
— alcaligenes	53
— alkalescens	80
— ambiguus	77
— amylobacter immobilis	117
— anaerobius alcaligenes	125
— anthracis	109
— bifermentans sporogenes	116
— bifidus	47
— botulinus	113
— bronchicanis	91
— bronchisepticus	91
— butyricus asporogenes immobilis	117
— butyricus putrefaciens	124
— capitovialis	121
— capsulatus aerogenes	117
— capsulatus-mucosus	59
— ceylonensis	81
— ceylonensis B	82
— cholerae	2
— cholerae-caviae	69
— cholerae-suis	71
— cloacae	56
— coli communis	54
— coli verus	54
— comma	2
— diaphthericus	120
— diphtheriae	48
— dispar	81, 82
— duplex	101
— duplex liquefaciens	102
— dysenteriae	76
— dysenteriae FLEXNER	79
— dysenteriae SCHMITZ	77
— dysenteriae SONNE	81
— dysentericus	76
— emphysematis vaginae	117
— emphysematosus	117
— enteritidis	73, 115
— enteritidis B, type murium	69
— enteritidis sporogenes	115
— erysipelatos suis	51
— erzincjan	70
— escherichii	54

B	
Bacillus faecalis alcaligenes	53
— fallax	110
— flexneri	79
— fluorescens	1
— fragilis	92
— friedlanderi	57
— funduliformis	93
— gaertner	73
— gintottensis	78
— gümtheri	39
— histolyticus	126
— influenzae	95
— japonicus	76
— lactantium	55
— lactis aerogenes	55
— lactis cloacae	56
— lacunatus	101
— lignieri	86
— mallei	85
— melitensis	88
— mirabilis	65
— monocytogenes	50
— morgani	66
— mucosus-capsulatus	57
— mucosus ozaenae	59
— murium	69
— novyi	112
— oedematis	112
— oedematis maligni	112
— oedematis thermophilus	112
— ozaenae	59, 85
— para-aertrycke	69
— para-colon	63
— paradysenteriae	79
— paraputrificus	120
— paraputrificus coli	120
— parasarcophysematos	111
— paratyphi	67
— paratyphi alcaligenes	68
— paratyphosus A	67
— paratyphosus B	68
— paratyphosus C	70
— pertussis	98
— pestis bubonicae	83
— pestis-caviae	69
— phlegmones emphysematosae	117
— pneumoniae	57
— pneumosintes	104
— proteus mirabilis	65
— proteus vulgaris	64
— pseudoramosus	65
— pullorum	74
— putrificus coli	124
— pyocyanus	1
— rhinoscleromatis	60
— rhusiopathiae suis	51
— ruboris suis	51
— salmoni	71
— schottmülleri	68
— septicus	111
— septicus ulceris gangraenosi	111
— shigae	76
— sporogenes	115
— sporogenes oedematis	116
— suipestifer	71
— suis	71
— tertius	127
— tetani	123
— tetanoides	122
— thermophilus	112
— thetoides	93
— thuillieri	51
— tuberculosis	128
— tularensis	84
— tumefaciens	111
— typhi abdominalis	72
— typhi murium	69
— typhosus	72
— ulceris cancerosi	99
— welchii	117
Bactériidie charbonneuse (anthrax)	109
Bacteridium anthracis	109
— aurantiacum	8
Bacterium abortivum	89
— abortus	89
— aegyptiacum	95
— aerogenes	55
— aerogenes capsulatus	117

The *italic numbers* in this index are reference numbers corresponding to the *italic numbers* in column 2 of the tables on pages 129-168. Further information on any pathogenic organism (synonyms, characteristics, vectors, diseases, susceptibility to antibiotics, etc.) or infectious disease listed may therefore readily be found by looking under the appropriate number in column 2 of the tables.

B

<i>Bacterium aertrycke</i>	69
— <i>aeruginosum</i>	1
— <i>alkalescens</i>	80
— <i>ambiguum</i>	77
— <i>anatis</i>	75
— <i>anatum</i>	75
— <i>anthracis</i>	109
— <i>bronchicanis</i>	91
— <i>bronchisepticus</i>	91
— <i>cholerae-suis</i>	71
— <i>cloacae</i>	56
— <i>coli commune</i>	54
— <i>conjunctivitis</i>	101
— <i>diphtheriae</i>	48
— <i>dysenteriae</i>	76
— <i>emphysematosus</i>	117
— <i>enteritidis</i>	73
— <i>enteritidis breslau</i>	69
— <i>erysipelatos suum</i>	51
— <i>erysipeloidis</i>	52
— <i>faecalis alcaligenes</i>	53
— <i>flexneri</i>	79
— <i>friedlander</i>	57
— <i>hirschfeldii</i>	70
— <i>influenzae</i>	95
— <i>intestinale suis</i>	71
— <i>lactis aerogenes</i>	55
— <i>mallei</i>	85
— <i>melitense</i>	88
— <i>metacoli</i>	66
— <i>monocytogenes</i>	50
— <i>morgani</i>	66
— <i>mucosum-capsulatum</i>	59
— <i>mucosus ozaena</i>	59
— <i>nasalis</i>	60
— <i>oedematis thermophilus</i>	112
— <i>paradysenteriae</i>	79
— <i>paratyphi</i>	67
— <i>paratyphosum A</i>	67
— <i>paratyphosum B</i>	68
— <i>pestis bubonicae</i>	83
— <i>pneumoniae</i>	30
— <i>pneumoniae crouposae</i>	57
— <i>pneumonicum</i>	57
— <i>pneumosintes</i>	104
— <i>proteus anindologenes</i>	64
— <i>proteus vulgaris</i>	64
— <i>psittacosis</i>	69
— <i>pullorum</i>	74
— <i>purificans</i>	86
— <i>pyocyaneum</i>	1
— <i>rhinoscleromatis</i>	60
— <i>rhysioopathiae suis</i>	51
— <i>schmitzii</i>	77
— <i>schottmülleri</i>	68
— <i>shigae</i>	76
— <i>sonnei</i>	81
— <i>suipestifer</i>	71
— <i>tuberculosis</i>	128
— <i>typhosum</i>	72
— <i>typhi</i>	69
— <i>typhi-murium</i>	72
— <i>ulceris cancrisi</i>	99
— <i>vulgare</i>	64
— <i>welchii</i>	117
<i>Bacteroides bifidus</i>	47
— <i>fragilis</i>	92
— <i>funduliformis</i>	93
<i>Bacteroidosis</i>	92, 93
<i>Bahia boil</i>	235
<i>Balantidium coli</i>	245
— <i>giganteum</i>	245
<i>Bandwürmer</i>	260-266
<i>BANG's disease</i>	89
<i>Bartonella bacilliformis</i>	175
— <i>coccoides</i>	175
— <i>peruviana</i>	175
<i>Bartonia bacilliformis</i>	175
<i>Beef tapeworm</i>	265
<i>Bilharzia haematobia</i>	256
— <i>magna</i>	256
<i>Bilharziasis</i>	256-258
<i>Black-water fever</i>	244
<i>Blanchet (moniliiasis)</i>	280
<i>Blastodendron erectum</i>	280
— <i>faurei</i>	280

B

<i>Blastodendron intestinale</i>	280
— <i>pinoyi</i>	280
<i>Blennorrhoea, inclusion</i>	177
<i>BOAS-OPPLER bacillus</i>	46
<i>Bodo asiaticus</i>	227
— <i>caudatus</i>	227
— <i>urinarius</i>	227
<i>Boils</i>	5
<i>BORDET-GENGOU bacillus</i>	98
<i>Bornholm disease</i>	201
<i>Borrelia carteri</i>	152
— <i>duttonii</i>	149
— <i>hermsi</i>	155
— <i>kochii</i>	150
— <i>novyi</i>	151
— <i>parkeri</i>	156
— <i>recurrentis</i>	148
— <i>refringens</i>	154
— <i>rossi</i>	150
— <i>turicatae</i>	157
— <i>venezuelensis</i>	158
— <i>vincentii</i>	153
<i>Borrelia variolae</i>	185
<i>Bothriocephalus latissimus</i>	260
— <i>taenoides</i>	260
<i>Botulism</i>	113
<i>Boussarole</i>	164
<i>Bouton d'Alep</i>	234
— <i>de Bahia</i>	235
— <i>de Delhi</i>	234
— <i>d'Orient</i>	234
<i>Boutonneuse fever</i>	171
<i>Brevistreptothrix israeli</i>	135
<i>Briareus morbillorum</i>	188
— <i>varicellae</i>	186
<i>BRILL's disease</i>	168
<i>Broad tapeworm</i>	260
<i>Bronchiectasis</i>	44
<i>Bronchitis</i>	30
<i>Bronchopneumonia</i>	30, 34, 91
<i>Brucella abortus</i>	89
— <i>bronchiseptica</i>	91
— <i>mallei</i>	85
— <i>melitensis</i>	88
— <i>melitensis var. suis</i>	90
— <i>suis</i>	90
— <i>tularensis</i>	84
<i>Brucellosis</i>	88-90
<i>BRUG's filaria</i>	269
<i>Bubo, climatic</i>	178
<i>Buboes</i>	84
<i>Bubonic plague</i>	83
<i>Butyribacillus immobilis-liquefaciens</i>	117
<i>Bwamba fever</i>	205

C

<i>Cacospora duttoni</i>	149
— <i>novyi</i>	151
— <i>obermeieri</i>	148
— <i>recurrentis</i>	148
<i>Calabar swellings</i>	270
<i>Calymmatobacterium granulomatis</i>	58
<i>Candida albicans</i>	280
— <i>pinoyisimilis</i>	280
<i>Cane sugar fever</i>	165-167
<i>Canicola fever</i>	167
<i>Carate</i>	164
<i>CARRION's disease</i>	175
<i>Caseococcus</i>	39
<i>Castellanus castellanii</i>	82
— <i>gintottensis</i>	78
— <i>kruse-castellani</i>	81
<i>Cat-scratch disease</i>	216
<i>Caudamoeba sinensis</i>	219
<i>Ceinturon de feu (herpes zoster)</i>	187
<i>Centrocestus armatus</i>	252
<i>Cercomonas crassicaudata</i>	225
— <i>hominis</i>	239
— <i>intestinalis</i>	240
<i>CHAGAS' disease</i>	231
<i>Chancroid</i>	99
<i>Charbon (anthrax)</i>	109
<i>Charente fever</i>	165 167
<i>Charon evegatus</i>	205
— <i>vallis</i>	207
<i>Chickenpox</i>	186
<i>Chilomastix granatensis</i>	239

C

<i>Chilomastix mesnili</i>	239
<i>Chlamydozoon oculogenitale</i>	177
— <i>trachomatis</i>	176
<i>Cholera</i>	2
<i>Cholera infantum</i>	3
<i>Cholera nostras</i>	3
<i>Cholera vibrio</i>	2
<i>Cholecystitis</i>	54
<i>Choriomeningitis, lymphocytic</i>	202, 203
<i>Cillobacterium multifforme</i>	117
<i>Cladascus mallei</i>	85
<i>Cladotrix actinomyces</i>	134
— <i>asteroides</i>	130
— <i>bovis</i>	134
— <i>madurae</i>	132
<i>Cladothrix des Erythema migrans</i>	52
<i>Climatic bubo</i>	178
<i>Cloaca cloacae</i>	56
<i>Clonorchis endemicus</i>	248
— <i>sinensis</i>	248
<i>Clostridium aerosolatum</i>	114
— <i>aerogenes-capsulatum</i>	117
— <i>alcaligenes</i>	125
— <i>balaenae</i>	111
— <i>bifermens</i>	116
— <i>botulinu</i>	113
— <i>capitovale</i>	121
— <i>centrosporogenes</i>	116
— <i>fallax</i>	110
— <i>flabelliferum</i>	115
— <i>foetidum</i>	116
— <i>histolyticum</i>	126
— <i>innominatum</i>	119
— <i>lentoputrescens</i>	124
— <i>novyi</i>	112
— <i>oedematis</i>	112
— <i>oedematoides</i>	116
— <i>paraputreficium</i>	120
— <i>parasporogenes</i>	115
— <i>perfringens</i>	117
— <i>phlegmones emphysematosae</i>	117
— <i>putrificum</i>	124
— <i>septicum</i>	111
— <i>sordelli</i>	116
— <i>sphenoides</i>	118
— <i>sporogenes</i>	115
— <i>sporogenes var. B</i>	116
— <i>tertium</i>	127
— <i>tetani</i>	123
— <i>tetanoides</i>	122
— <i>thermophilum</i>	112
— <i>tumefaciens</i>	111
— <i>welchii</i>	117
<i>Coccobacillus ducreyi</i>	99
— <i>friedlander</i>	57
— <i>pfeifferi</i>	95
— <i>yersini</i>	83
<i>Coccobacterium tularense</i>	84
<i>Cocciobrix leprae</i>	129
— <i>tuberculosis</i>	128
<i>Coccus acidoproteolyticus casei</i>	39
<i>Coccus lancéolé</i>	30
<i>Coco</i>	160
<i>Coeliac disease</i>	240
<i>Coenogonimus heterophyes</i>	250
<i>Cohnistreptothrix bifidus</i>	47
— <i>bronchitica</i>	135
— <i>israeli</i>	135
<i>Cold, common</i>	212
<i>Colibacillus</i>	54
<i>Colloides anoxydana</i>	108
<i>Colobactrum aerogenes</i>	55
— <i>coli</i>	54
<i>Comma bacillus</i>	2
<i>Conjunctivitis</i>	30, 95, 101, 102, 106-108, 177
— <i>angular</i>	101
— <i>inclusion</i>	177
— <i>infantile</i>	177
— <i>swimming pool</i>	177
<i>Coqueluche (whooping cough)</i>	98
<i>Cornea, ulceration</i>	102
<i>Cornelia pasteurii</i>	111
<i>Corynebacterium abortus endemici</i>	89
— <i>acnes</i>	49
— <i>diphtheriae</i>	48
— <i>israeli</i>	135
— <i>mallei</i>	85
— <i>parvulum</i>	50

The *italic numbers* in this index are reference numbers corresponding to the *italic numbers* in column 2 of the tables on pages 129–168. Further information on any pathogenic organism (synonyms, characteristics, vectors, diseases, susceptibility to antibiotics, etc.) or infectious disease listed may therefore readily be found by looking under the appropriate number in column 2 of the tables.

C	
<i>Cotyllogonimus heterophyes</i>	250
Cowpox	185
<i>Coxiella burnetii</i>	174
Coxsackie virus	201
CRUCHET's disease	195
<i>Cryptococcus copellii</i>	280
<i>Cyathomastix hominis</i>	239
Cysticercosis	264
Cystitis	11, 54, 64–66

D	
Delhi sore	234
Dengue	206
<i>Dermacentroxenus conori</i>	171
— <i>orientalis</i>	172
— <i>rickettsi</i> var. <i>brasiliensis</i>	170
— <i>rickettsi</i> var. <i>conori</i>	171
— <i>rickettsi</i> var. <i>pijperi</i>	171
— <i>typhi</i>	169
<i>Dialister granuliformans</i>	105
— <i>pneumosintes</i>	104
Diarrhoea (bacteria)	64–68, 81
— (worms)	246, 248, 249, 259, 267, 272–274
<i>Dibothriocephalus latus</i>	260
<i>Dibothrium latum</i>	260
<i>Dientamoeba fragilis</i>	224
<i>Difoemus tunensis</i>	239
Diphtheria	34, 35, 48
<i>Diphyllobothrium erinacei</i>	261
— <i>latum</i>	260
— <i>mansoni</i>	261
<i>Diplobacillus liquefaciens</i>	102
— <i>moraxaxenfeld</i>	101
<i>Diplococcus constellatus</i>	33
— <i>enterococcus</i>	38
— <i>gonorrhoeae</i>	15
— <i>intracellularis</i>	16
— <i>intracellularis meningitidis</i> WEICHELBAUM	16
— <i>lanceolatus capsulatus</i>	30
— <i>meningitidis</i>	16
— <i>paleopneumoniae</i>	31
— <i>pharyngis communis</i>	17
— <i>pharyngis siccus</i>	18
— <i>plagarum-belli</i>	32
— <i>pneumoniae</i>	30
— <i>reniformis</i>	24
Diplocoque	30
<i>Dipylidium caninum</i>	262
— <i>cucumerinum</i>	262
<i>Discomyces asteroides</i>	130
— <i>bovis</i>	134
— <i>indicus</i>	132
— <i>israeli</i>	135
— <i>leishmani</i>	131
— <i>leprae</i>	129
— <i>lignieresii</i>	86
— <i>madurae</i>	132
— <i>pelletieri</i>	139
— <i>rosenbachi</i>	52
— <i>somaliensis</i>	146
— <i>tuberculosis</i>	128
Distemper	91
<i>Distoma (Distomum) buski</i>	246
— <i>capense</i>	256
— <i>crassum</i>	246
— <i>heterophyes</i>	250
— <i>pulmonale</i>	247
— <i>sinense</i>	248
— <i>spatulatum</i>	248
<i>Dochmius duodenalis</i>	275
DONOVAN bodies	87
— organism	87
<i>Donovania granulomatis</i>	87
<i>Douglasillus sphenoides</i>	118
Dracunculosis	272
<i>Drancunculus loa</i>	270
— <i>medinensis</i>	272
— <i>oculi</i>	270
Dumdum fever	232
Dwarf tapeworm	263
Dysentery (amoeba)	219, 224
— (bacteria)	76–82
— (Balantidium)	245

E	
Ear, middle, infections	36, 57
EBERTH's bacillus	72

E	
<i>Eberthella alkalescens</i>	80
— <i>ambigua</i>	77
— <i>dispar</i>	82
— <i>dysenteriae</i>	76
— <i>flexneri</i>	79
— <i>paradysenteriae</i>	79
— <i>typhosa</i>	72
<i>Eberthus typhosus</i>	72
<i>Echinococcifer echinococcus</i>	266
<i>Echinococcus alveolaris</i>	266
— <i>granulosus</i>	266
— <i>multilocularis</i>	266
— <i>polymorphus</i>	266
<i>Echinostoma (-um) ilocanum</i>	253
— <i>malayanum</i>	255
ECONOMO's disease	195
Edema. See Oedema.	
Eelworm	278
<i>Ehrlichia bronchopneumoniae</i>	182
— <i>lymphogranulomatis</i>	178
— <i>psittaci</i>	179
Einsiedlerbandwurm	264
El Tor	2
El Tor vibrio	2
Elephantiasis	268, 269
<i>Embadomonas intestinalis</i>	226
<i>Encapsulatus lactis-aerogenes</i>	55
— <i>ozanae</i>	59
— <i>pneumoniae</i>	57
Encephalitis	192–199
— benign	192
— forest spring	193
— lethargic	195
— poliomyelitis	194
— Russian spring summer	193
— St. Louis	198
— sheep	192
— spring	193, 196
— vernal	193
— West Nile	197
Encephalomyelitis, equine	199
Endocarditis	5, 30–39
<i>Endolimax nana</i>	222
— <i>pileonucleatus</i>	223
— <i>williamsi</i>	223
<i>Endomyces albicans</i>	280
<i>Entamoeba africana</i>	219
— <i>coli</i>	220
— <i>confusa</i>	221
— <i>dysenteriae</i>	219
— <i>gingivalis</i>	221
— <i>histolytica</i>	219
— <i>hominis</i>	220
— <i>macrohyalina</i>	221
— <i>minuta</i>	219
— <i>nipponica</i>	220
— <i>nuttalli</i>	219
— <i>schaudinni</i>	219
— <i>tetragena</i>	219
— <i>urogenitalis</i>	219
— <i>williamsi</i>	220
Enteritis	1, 61, 67, 70, 71, 73, 75
<i>Enterobius vermicularis</i>	279
<i>Enterococcus proteiformis</i>	38
Entérocoque	38
<i>Enteromonas hominis</i>	228
Eosinophilia	267, 272, 274–278
<i>Eperthyrozoön noguchii</i>	175
Epithelial cell parasites DONOVAN	87
Erkältung (common cold)	212
<i>Ermengemillus botulinus</i>	113
Erosio interdigitalis	280
<i>Erro equinus</i>	199
— <i>incognitus</i>	194
— <i>japonicus</i>	196
— <i>nili</i>	197
— <i>scelestus</i>	198
— <i>scoticus</i>	192
— <i>silvestris</i>	193
Erysipelas	34, 35
Erysipeloid	51, 52
<i>Erysipelothrix erysipelatos suis</i>	51
— <i>erysipeloidis</i>	52
— <i>rhusiopathiae</i>	51
Erythema arthriticum epidemicum	100
<i>Escherichia anata</i>	75
— <i>coli</i>	54
— <i>morgani</i>	66

E	
Espundia	235
Esthiomene	178
<i>Eucystia pestis</i>	83
<i>Eumyces tuberculosis</i>	128
<i>Euparyphium ilocanum</i>	253
— <i>jassyense</i>	254
— <i>malayanum</i>	255
— <i>melio (melis)</i>	254
Eye worm, African	270

F	
<i>Fanapepea intestinalis</i>	239
<i>Fascioletta ilocana</i>	253
<i>Fasciolopsis buski</i>	246
— <i>fülleborni</i>	246
Febris undulans	88–90
Felons	5
Fever, black-water	244
— boutonneuse	171
— cane-sugar	165–167
— canicola	167
— Charente	165–167
— dum dum	232
— field	165–167
— five-day	173
— flood	172
— Fort Bragg	165–167
— haemorrhagic	217
— harvest	165–167
— Haverhill	100
— Japanese autumn	165–167
— Japanese river	172
— Japanese seven-day	165–167
— Kedani	172
— leptospiral	165–167
— Malta	88
— Manchurian	217
— marsh	165–167
— Mediterranean	171
— mud	165–167
— Oroya	175
— pappatici	210
— parrot	179
— puerperal	10, 34, 35, 40, 42–44, 93
— Q	174
— quadrilateral	174
— Queensland	174
— quintan	173
— rat-bite	4, 100
— relapsing	148–152, 155–158
— rheumatic	34–35
— Rift Valley	207
— rock	88
— Rocky Mountain spotted	170
— sandfly	210
— scarlet	29, 34
— swamp	165–167
— three-day	201
— tibialgic	165–167, 173
— tick	149
— Tobia	170
— trench	173
— typhoid	72
— typhus	168–172
— undulant	88–90
— Volhynia	173
— yellow	205
FIEDLER's disease	165
Field fever	165–167
Filaria	268–272
<i>Filaria aethiopica</i>	272
— <i>bancrofti</i>	268
— <i>bourgi</i>	270
— <i>diurna</i>	270
— <i>loa</i>	270
— <i>medinensis</i>	272
— <i>nocturna</i>	268
— <i>oculi</i>	270
— <i>philippinensis</i>	268
— <i>sanguinis hominis</i>	268
— <i>sanguinis hominis maior</i>	270
— <i>volvulus</i>	271
Filariasis	268–272
Fish tapeworm	260
Fistula	256–258
Five-day fever	173

The *italic numbers* in this index are reference numbers corresponding to the *italic numbers* in column 2 of the tables on pages 129-168. Further information on any pathogenic organism (synonyms, characteristics, vectors, diseases, susceptibility to antibiotics, etc.) or infectious disease listed may therefore readily be found by looking under the appropriate number in column 2 of the tables.

F

Flecktyphus (typhus)	168-170
Flood fever	172
Food poisoning	64, 67-71, 73, 113
Foot and mouth disease	209
<i>Formido inexorabilis</i>	204
Fort Bragg fever	165-167
<i>Fossilis quintana</i>	173
Fowl plague	208
Frambesia	160
FRIEDLAENDER's bacillus	57
Fungi	280
<i>Fusarella vermicularis</i>	279
<i>Fusiformis acnes</i>	49
— <i>fragilis</i>	92
— <i>plauti-vincenti</i>	94
— <i>vincenti</i>	94
<i>Fusobacterium plauti-vincenti</i>	94

G

<i>Gaffkya anaerobia</i>	13
— <i>tetragena</i>	12
Gallbladder infections	36, 240
Gangrene, gas	42, 110-121
— moist	40, 126, 127
— pulmonary	25, 26, 41-44, 92, 93
GÄRTNER's bacillus	73
Gas gangrene	42, 110-121
<i>Gastrodiscoides hominis</i>	259
Gastroenteritis	71
<i>Geotrichoides krusei</i>	280
— <i>tumefaciens</i>	280
<i>Giardia enterica</i>	240
— <i>intestinalis</i>	240
Giki-yami	166
Glanders	85
Gonococcus	15
Gonorrhoea	15
Granuloma inguinale	58, 87
Grippe	211
— summer	201
Guinea worm	272
Gürtelrose (herpes zoster)	187
<i>Gynaecophorus haematobius</i>	256

H

Haarschopf	273
<i>Haemamoeba malariae</i>	243
— <i>praecox</i>	244
— <i>vivax</i>	242
<i>Haemophilus conjunctivitis</i>	95
— <i>ducreyi</i>	99
— <i>duplex</i>	101
— <i>haemolyticus</i>	96
— <i>influenzae</i>	12, 95
— <i>lacunatus</i>	101
— <i>meningitidis cerebrospinalis septicaemiae</i>	95
— <i>parainfluenzae</i>	97
— <i>pertussis</i>	98
Haemorrhagic fever	217
<i>Haemosporidium quartanae</i>	243
Harvest fever	165-167
Haverhill fever	100
<i>Haverhillia multiformis</i>	100
Heart, enlargement	275
HEINE-MEDIN disease	200
<i>Hemophilus</i> . See <i>Haemophilus</i> .	
<i>Henrillus tertius</i>	127
Hepatitis	207, 214, 215, 219
— enzootic	207
— haematogenic	215
— infective	214
— inoculation	215
— serum	215
<i>Herellea vaginicola</i>	107
Herpangina	201
Herpes febrilis	189
— simplex	189
— zoster	187
<i>Heterophyes heterophyes</i>	250
— <i>katsuradai</i>	251
— <i>yokogawai</i>	249
<i>Hexamitus duodenalis</i>	240
Hookworm	275-277
<i>Hostis pecoris spec. nov.</i>	209
Hundestaupe (distemper)	91

H

<i>Hyalococcus pneumoniae</i>	57
Hydatid cysts	266
— tapeworm	266
Hydrophobia	204
<i>Hymenolepis nana</i>	263

I

Icterohaemoglobinuria, cattle	165-167
Illinois pneumonia	184
<i>Indiella somaliensis</i>	146
<i>Indiellopsis somaliensis</i>	146
Influenza	34, 35, 104, 105, 211
Inoculation hepatitis	215
<i>Iodamoeba bütschlii</i>	223
— <i>williamsi</i>	223

J

Japanese autumn fever	165-167
— river fever	172
— seven-day fever	165-167
Jaundice, leptospiral	165
— spirochaetal	165
Jericho boil (Aleppo boil)	234

K

Kala-azar	232, 233
Kedani fever	172
Keratitis, dendritic	189
Keuchhusten (whooping cough)	98
Kinderlähmung (poliomyelitis)	200
KLEBS-LOEFFLER bacillus	48
<i>Klebsiella crouposa</i>	57
— <i>enteritidis</i>	73
— <i>friedlander</i>	57
— <i>granulomatis</i>	58
— <i>ozanae</i>	59
— <i>pneumoniae</i>	57
— <i>rhinoscleromatis</i>	60

L

<i>Lactobacillus acidophilus</i>	46
— <i>bifidus</i>	47
<i>Lambliia intestinalis</i>	240
Lamblia	240
<i>Lankoides ceylonensis B</i>	82
— <i>gintottensis</i>	78
<i>Laverania malariae</i>	244
— <i>praecox</i>	244
<i>Legio debilitans</i>	200
— <i>erebea</i>	202
— <i>simulans</i>	203
<i>Leishmania brasiliensis (brasiliensis)</i>	235
— <i>donovani</i>	232
— <i>furunculosa</i>	234
— <i>infantum</i>	233
— <i>peruviana</i>	235
— <i>tropica</i>	234
Leishmaniasis, infantile	233
— mucocutaneous	234, 235
— visceral	232
Leprosy	129
<i>Leptospira australis A</i>	165-167
— <i>australis B</i>	165-167
— <i>autumnalis</i>	165-167
— <i>bovis</i>	165-167
— <i>canicola</i>	165-167
— <i>grippotyphosa</i>	165-167
— <i>hebdomadis</i>	165-167
— <i>icterogenes</i>	165
— <i>icterohaemorrhagiae</i>	165
— <i>mitis</i>	165-167
— <i>nodosa</i>	165-167
— <i>pomona</i>	165-167
— <i>pyrogenes</i>	165-167
Leptospiral fever	165-167
Leptospirosis	165-167
Leucocytosis	267, 274, 275
<i>Listerella hepatolytica</i>	50
— <i>monocytogenes hominis</i>	50
<i>Listeria monocytogenes</i>	50
Liver, enlargement	248
<i>Loa loa</i>	270
Lockjaw	123
<i>Loefflerella mallei</i>	85

L

Louisiana pneumonia	183
<i>Loxotrema ovatum</i>	249
Lungs, infections	36, 37
Lungenpest (pneumonic plague)	83
Lymphadenitis	216
Lymphogranuloma inguinale	178
— venereal	178
Lymphoreticulosis benigna	216
Lyssa	204

M

<i>Macrostoma mesnili</i>	239
Madura foot	132
Maduramycosis	132
Mal de los Pintos	164
Malaria	242-244
<i>Malleomyces mallei</i>	85
Malta fever	88
<i>Mammococcus</i>	39
Manchurian fever	217
Marsh fever	165-167
<i>Martellillus bifementans</i>	116
Masern (measles)	34, 35, 188
Mastitis	5
Mastoiditis	5
Maul- und Klauenseuche	209
Measles	34, 35, 188
Medina worm	272
Mediterranean fever	171
<i>Megastoma entericum</i>	240
— <i>intestinale</i>	240
Meningitis	1, 16, 30, 95, 180
— epidemic cerebrospinal	16
Meningococcus	16
<i>Meningococcus intracellularis</i>	16
Meningoencephalitis	201
Meningopneumonitis	180
<i>Merismopedia gonorrhoeae</i>	15
— <i>goodsirii</i>	14
— <i>ventriculi</i>	14
<i>Mesogonimus heterophyes</i>	250
— <i>westermanni (westermanni)</i>	247
<i>Metagonimus yokogawai</i>	249
<i>Microbacterium multiforme psittacosis</i>	179
<i>Micrococcus aerogenes</i>	10
— <i>albus</i>	6
— <i>alcalescens</i>	26
— <i>anaerobius</i>	11
— <i>aurantiacus</i>	8
— <i>aureus</i>	5
— <i>casei amari</i>	39
— <i>catarrhalis</i>	17
— <i>citreus</i>	7
— <i>epidermidis</i>	9
— <i>albus</i>	9
— <i>erysipelatis</i>	34
— <i>foetidus</i>	41
— <i>gazogenes alcalescens anaerobius</i>	26
— <i>gingivalis</i>	27
— <i>gonococcus</i>	15
— <i>gonorrhoeae</i>	15
— <i>intracellularis</i>	16
— <i>lactis varians</i>	5
— <i>melitensis</i>	88
— <i>meningococcus cerebrospinalis</i>	16
— <i>minutissimus</i>	28
— <i>parvulus</i>	25
— <i>pasteuri</i>	30
— <i>pelletieri</i>	139
— <i>pharyngis siccus</i>	18
— <i>pneumoniae crouposae</i>	30
— <i>pyocyaneus</i>	1
— <i>pyogenes var. albus</i>	6
— <i>pyogenes var. aureus</i>	5
— <i>pyogenes citreus</i>	7
— <i>pyogenes tenuis</i>	30
— <i>reniformis</i>	24
— <i>scarlatinae</i>	34
— <i>syzygios</i>	29
— <i>syzygios scarlatinae</i>	29
— <i>tetragenus</i>	12
— <i>tetragenus anaerobius</i>	13
<i>Microspira finkleri</i>	3
— <i>protea</i>	3
<i>Microspironema pallidum</i>	159
<i>Microsporon dipthericum</i>	48
Millet (moniliasis)	280

Index of Pathogenic Organisms (Bacteria, Protozoa, Worms) and Infectious Diseases (continued)

The *italic numbers* in this index are reference numbers corresponding to the *italic numbers* in column 2 of the tables on pages 129-168. Further information on any pathogenic organism (synonyms, characteristics, vectors, diseases, susceptibility to antibiotics, etc.) or infectious disease listed may therefore readily be found by looking under the appropriate number in column 2 of the tables.

M

Milzbrand (anthrax)	109
<i>Mima polymorpha</i>	106
Minas Gerais typhus	170
Mite-borne typhus	172
<i>Miyagawanella bronchopneumoniae</i>	182
— <i>ilini</i>	184
— <i>louisianae</i>	183
— <i>lymphogranulomatis</i>	178
— <i>ornithosis</i>	180
— <i>pneumoniae</i>	181
— <i>psittaci</i>	179
<i>Molitor hominis</i>	191
— <i>verrucae</i>	190
Molluscum contagiosum	191
<i>Monilia albicans</i>	280
Moniliids	280
<i>Monocercomonas hominis</i>	236
Mononucleosis, infectious	50
<i>Moraxella duplex liquefaciens</i>	102
— <i>lacunata</i>	101
— <i>liquefaciens</i>	102
Morbilli	188
<i>Morganella morganii</i>	66
MORGAN's bacillus No. 1	66
Morve (glanders)	85
Mud fever	165-167
Muguet (moniliasis)	280
Mumps	218
<i>Mycobacterium leprae</i>	129
— <i>mallei</i>	85
— <i>rhusiopathiae</i>	51
— <i>tuberculosis</i>	128
<i>Mycotorula actoni</i>	280
— <i>alba</i>	280
— <i>albicans</i>	280
— <i>alvarezsotoi</i>	280
— <i>armeniensis</i>	280
— <i>bethaliensis</i>	280
— <i>buccalis</i>	280
— <i>decolorans</i>	280
— <i>faecalis</i>	280
— <i>glycophila</i>	280
— <i>harteri</i>	280
— <i>inexorabilis</i>	280
— <i>laryngitidis</i>	280
— <i>mannitofermentans</i>	280
— <i>metalondinensis</i>	280
— <i>nabarroi</i>	280
— <i>oosporoides</i>	280
— <i>ovalis</i>	280
— <i>perinquealis</i>	280
— <i>pseudo-albicans</i>	280
— <i>pseudo-londinensis</i>	280
— <i>pseudo-londinoides</i>	280
— <i>psilosis</i>	280
— <i>quasilinguae-pilosae</i>	280
— <i>rboi</i>	280
— <i>richmondi</i>	280
— <i>vaginalis</i>	280
— <i>verticillata</i>	280

N

Nanuka-yami	165-167
<i>Necator americanus</i>	277
— <i>argentinus</i>	277
<i>Neisseria catarrhalis</i>	17
— <i>discoidea</i>	23
— <i>flava</i>	20
— <i>flavescens</i>	22
— <i>gonorrhoeae</i>	15
— <i>intracellularis</i>	16
— <i>meningitidis</i>	16
— <i>perflava</i>	19
— <i>pharyngis-sicci</i>	18
— <i>reniformis</i>	24
— <i>sicca</i>	18
— <i>subflava</i>	21
— <i>weichselbaumii</i>	16
<i>Nemathelminthes</i>	267-279
<i>Neurocystis herpetii</i>	189
Newcastle disease	208
NICOLAS-FAVRE disease	178
<i>Nicolaierillus tetani</i>	123
<i>Nocardia actinomycetes</i>	134
— <i>asteroides</i>	130
— <i>bifida</i>	47
— <i>bovis</i>	134

N

<i>Nocardia israeli</i>	135
— <i>leishmanii</i>	131
— <i>lignieresii</i>	86
— <i>lutea</i>	133
— <i>madurae</i>	132
— <i>pelletieri</i>	139
— <i>rosenbachii</i>	52
— <i>somaliensis</i>	146
— <i>sulphurea</i>	134
— <i>thuyllieri</i>	51
<i>Noguchia granulosis</i>	103
<i>Novillus maligni</i>	112

O

Oedema	246, 267, 274, 275
Oidiomycosis	280
<i>Oidium albicans</i>	280
OLMER's disease	171
<i>Onchocerca volvulus</i>	271
<i>Oospora asteroides</i>	130
— <i>erysipeloidis</i>	52
— <i>indica</i>	132
— <i>israeli</i>	135
— <i>madurae</i>	132
— <i>pelletieri</i>	139
— <i>rosenbachii</i>	52
Ophthalmoblenorrhoea	15
<i>Opisthorchis buskii</i>	246
— <i>sinensis</i>	248
Orchitis, mumps-	218
Oreillons (mumps)	218
Oriental button	234
Ornithosis	180
Oroya fever	175
<i>Oscillaria malariae</i>	243
Osteomyelitis	5, 42
Otitis media	5, 30, 34, 64, 93
<i>Oxyuris vermicularis</i>	279
Ozaena	59

P

<i>Pacinia finkleri</i>	3
— <i>loeffleri</i>	48
— <i>putrificans</i>	124
— <i>tetani</i>	123
<i>Palmula alcaligenes</i>	125
— <i>macrospora</i>	122
— <i>spermoides</i>	127
Paludism	242-244
Pancreatitis	218
Pappataci fever	210
<i>Para-aerogenes</i>	61
<i>Para-coli</i>	63
<i>Paracolon bacilli</i>	61-63
<i>Para-fremdii</i>	62
<i>Paragonimus ringeri</i>	247
— <i>westermanni</i> (westermanni)	247
— <i>yokogawai</i>	249
Paralysis, infantile	200
Parangi	160
<i>Parasaccharomyces harteri</i>	280
Paratyphoid	67, 68
Paronychia	5, 51
Parotitis	218
Parrot fever	179
<i>Pasteurella lignieresii</i>	86
— <i>pestis</i>	83
— <i>pestis-caviae</i>	69
— <i>purificans</i>	86
— <i>thuyllieri</i>	51
— <i>tularensis</i>	84
Patek	160
Pea-pickers' disease	165-167
<i>Pediococcus aurantiacus</i>	8
— <i>tetragnus</i>	12
Peitschenwurm	273
Pemphigus neonatorum	5
<i>Pentatrichomonas ardin-delteli</i>	236
Peritonitis	54, 64-66, 278
Perniciosa (malaria)	244
Pertussis	98
Pest (plague)	83
PEIFFER's bacillus	95

P

<i>Pfeifferella mallei</i>	85
Pfriemenschwanz	279
Phlegmon, perinephritic	41
Pian	160
Pinta, pinto	164
Pinworm	279
Plague	83
<i>Plasmodium falciparum</i>	244
— <i>immaculatum</i>	244
— <i>malariae</i>	243
— <i>praecox</i>	244
— <i>quartanae</i>	243
— <i>quotidianum</i>	244
— <i>tenuis</i>	244
— <i>tertiana</i>	242
— <i>vivax</i>	242
Platyhelminthes	246-266
<i>Plectridium capitovale</i>	121
— <i>gazogenes</i>	127
— <i>paraputrificum</i>	120
— <i>putrificum</i>	124
— <i>sphenoides</i>	118
— <i>tetani</i>	123
Pleurisy	44
<i>Placombacterium acidophilum</i>	46
Pneumococcus	30
<i>Pneumococcus pneumoniae</i>	30
Pneumonia 30, 31, 57, 180-184, 211, 267, 275, 278	
Pocken (smallpox)	185
Polioencephalitis	194
Poliomyelitis	200
<i>Pollendera anthracis</i>	109
Polyarthritis rheumatica	34, 35
Pork tapeworm	264
<i>Proactinomyces asteroides</i>	130
— <i>bovis</i>	134
— <i>israeli</i>	135
<i>Propionibacterium acnes</i>	49
<i>Prothigella alkaliscens</i>	80
— <i>sonnei</i>	81
<i>Proteus mirabilis</i>	65
— <i>morganii</i>	66
— <i>pneumoniae</i>	57
— <i>vulgaris</i>	64
<i>Protomycetum recurrentis</i>	148
Protozoa	219-245
<i>Prowazekia cruzi</i>	227
<i>Pseudalius trichina</i>	274
Pseudochoiromeningitis, lymphocytic	203
Pseudodysenteriebazillus E, KRUSE	81
<i>Pseudolimax bütschlii</i>	223
— <i>wenyoni</i>	223
<i>Pseudomonas aeruginosa</i>	1
Pseudotuberculosis, Delhi	172
Psittacosis	179
Puerperal fever	10, 34, 35, 40, 42-44, 93
Purpura	16
<i>Putribacillus vulgaris</i>	124
Pyelitis	5, 64-66
Pyelonephritis	5, 54

Q

Q fever	174
Quadrilateral fever	174
Quartana (malaria)	243
Queensland fever	174
Quintan fever	173
Quotidiana (malaria)	244

R

Rabies	204
<i>Rabula inflans</i>	218
Rage (rabies)	204
Rat-bite fever	4, 100
Refroidissement (common cold)	212
Relapsing fever	148-152, 155-158
— African	149, 150
— American	151, 155-158
— European	148
— Indian	152
Respiratory tract, infections	17, 95, 105
<i>Rhabdonema intestinale</i>	267
— <i>stercorale</i>	267
— <i>strongyloides</i>	267
Rhinoscleroma	60
<i>Rickettsia akamushi</i>	172

The *italic numbers* in this index are reference numbers corresponding to the *italic numbers* in column 2 of the tables on pages 129-168. Further information on any pathogenic organism (synonyms, characteristics, vectors, diseases, susceptibility to antibiotics, etc.) or infectious disease listed may therefore readily be found by looking under the appropriate number in column 2 of the tables.

R

<i>Rickettsia blanchi</i>	171
— <i>brasiliensis</i>	170
— <i>conorii</i>	171
— <i>dermacentroxenus</i>	170
— <i>exanthematofebri</i>	169
— <i>exanthematotyphi</i>	168
— <i>fletcheri</i>	169
— <i>manchuriae</i>	169
— <i>megawi</i>	171
— <i>megawi var. fletcheri</i>	172
— <i>mooseri</i>	169
— <i>muricola</i>	169
— <i>murina</i>	169
— <i>orientalis</i>	172
— <i>provaazeki</i>	168
— <i>pseudotyphi</i>	172
— <i>psittaci</i>	179
— <i>quintana</i>	173
— <i>rickettsii</i>	170
— <i>trachomae</i>	176
— <i>trachomatis</i>	176
— <i>tsutsugamushi</i>	172
— <i>tsutsugamushi-orientalis</i>	172
— <i>typhi</i>	169
— <i>wolhynica</i>	173
Rift Valley fever	207
Rinderbandwurm	265
Rindertuberkulose	128
<i>Ristella fragilis</i>	92
<i>Rivoltillus vibron</i>	111
Rock fever	88
Rocky Mountain spotted fever	170
Rotzkrankheit (glanders)	85
Rougeole (measles)	188
Roundworm	278
Rubella	188
Rückfallfieber (relapsing fever)	148-152, 155-158
Ruhr (dysentery)	76-82, 219, 224, 245

S

<i>Saccharomyces albicans</i>	280
<i>Salmonella anatis</i>	75
— <i>anatum</i>	75
— <i>anatum var. aertrycke</i>	69
— <i>breslau</i>	69
— <i>choleraesuis</i>	71
— <i>enteritidis</i>	73
— <i>birschfeldii</i>	70
— <i>morgani</i>	66
— <i>paratyphi</i>	67
— <i>paratyphi A</i>	67
— <i>paratyphi B</i>	68
— <i>paratyphi C</i>	70
— <i>paratyphosus C</i>	70
— <i>psittacosis</i>	69
— <i>pullorum</i>	74
— <i>schottmuelleri</i>	68
— <i>suipestifer</i>	71
— <i>typhimurium</i>	69
— <i>typhosa</i>	72
Sandfly fever	210
São Paulo typhus	170
<i>Sarcina aurantiaca</i>	8
— <i>beijerinckii</i>	14
— <i>tetragena</i>	12
— <i>ventriculi</i>	14
Scarlatine (scarlet fever)	29, 34
Scarlet fever	29, 34
<i>Scelus recurrens</i>	189
Scharlach (scarlet fever)	29, 34
<i>Schistosoma (-um) haematobium</i>	256
— <i>cattol</i>	257
— <i>japonicum</i>	257
— <i>mansoni</i>	258
Schistosomiasis	256-258
<i>Schizotrypanum cruzi</i>	231
Schlafkrankheit (sleeping sickness)	229, 230
SCHMITZ's bacillus	77
Schweinebandwurm	264
<i>Sclerothrix kochii</i>	128
— <i>leprae</i>	129
— <i>mallei</i>	85
— <i>tuberculosis</i>	128
Scrub fever	172
Seatworm	279
<i>Seguinillus aérofoetidus</i>	114
Sepsis	16
Septicaemia	5, 6, 16, 55, 92, 93

S

Serum hepatitis	215
<i>Shigella alcalescens</i>	80
— <i>ambigua</i>	77
— <i>ceylonensis</i>	82
— <i>dysenteriae</i>	76
— <i>flexneri</i>	79
— <i>gintottensis</i>	78
— <i>paradysenteriae</i>	79
— <i>paradysenteriae var. sonnei</i>	81
— <i>schmitzii</i>	77
— <i>sonnei</i>	81
Shimamushi typhus	172
Shingles	187
Sinus infections	5, 36, 37
Skin infections	5, 8
— lesions	9
Sleeping sickness	195
— African	229, 230
Smallpox	185
Sodoku	4
Soor (moniliasis)	280
<i>Sparganum mansoni</i>	261
<i>Sphaerotilus bovis</i>	134
<i>Spherophorus funduliformis</i>	93
<i>Spirilla morsus muris</i>	4
— <i>muris</i>	4
<i>Spirillum carteri</i>	152
— <i>cholerae asiaticae</i>	2
— <i>duttoni</i>	149
— <i>finkleri</i>	3
— <i>minor</i>	4
— <i>minus</i>	4
— <i>obermeieri</i>	148
— <i>recurrentis</i>	148
<i>Spirochaeta calligra</i>	162
— <i>carteri</i>	152
— <i>duttoni</i>	149
— <i>genitalis</i>	163
— <i>hebdomadis</i>	166
— <i>hermsi</i>	155
— <i>icterohaemorrhagiae</i>	165
— <i>japonica</i>	4
— <i>kochi</i>	150
— <i>laverani</i>	4
— <i>morsus muris</i>	4
— <i>mucosa</i>	161
— <i>muris</i>	4
— <i>nanukayami</i>	166
— <i>nodosa</i>	165
— <i>novyi</i>	151
— <i>obermeieri</i>	148
— <i>pallida</i>	159
— <i>pallidula</i>	160
— <i>parkeri</i>	156
— <i>pertenuis</i>	160
— <i>pettiti</i>	4
— <i>plaut-vincenti</i>	153
— <i>recurrentis</i>	148
— <i>refringens</i>	154
— <i>rossi</i>	150
— <i>schaudinni</i>	153
— <i>sodoku</i>	4
— <i>turicatae</i>	157
— <i>vincenti</i>	153
<i>Spirochaeta carteri</i>	152
— <i>duttoni</i>	149
— <i>kochii</i>	150
— <i>laverani</i>	4
— <i>minor</i>	4
— <i>novyi</i>	151
— <i>obermeieri</i>	148
— <i>pallidum</i>	159
— <i>pertenuis</i>	160
— <i>recurrentis</i>	148
— <i>refringens</i>	154
— <i>vincenti</i>	153
<i>Spiroschaudinnia carteri</i>	152
— <i>duttoni</i>	149
— <i>hebdomadis</i>	166
— <i>icterohaemorrhagiae</i>	165
— <i>morsus muris</i>	4
— <i>novyi</i>	151
— <i>obermeieri</i>	148
— <i>recurrentis</i>	148
— <i>refringens</i>	154
— <i>rossii</i>	150
— <i>schaudinni</i>	153
— <i>vincenti</i>	153

S

Spitzpocken (chickenpox)	186
Splenomegaly	256-258
Spotted sickness	164
Sprue	240
Spulwurm	278
<i>Stannosoma armatum</i>	252
Staphylococcus	5
<i>Staphylococcus aerogenes</i>	10
— <i>albus</i>	6
— <i>anaerobius</i>	11
— <i>aurantiacus</i>	8
— <i>aureus</i>	5
— <i>epidermidis albus</i>	9
— <i>erysipelatos</i>	34
— <i>parvulus</i>	25
— <i>pyogenes</i>	5
— <i>pyogenes albus</i>	6
— <i>pyogenes aureus</i>	5
— <i>pyogenes citreus</i>	7
— <i>tetragenus</i>	12
Starrkrampf (tetanus)	123
Stillbirth	275
Stomatitis, aphthous	189
<i>Streptobacillus moniliformis</i>	100
<i>Streptococcus anaerobius</i>	40
— <i>anaerobius micro</i>	43
— <i>apis</i>	39
— <i>aurantiacus</i>	8
— <i>cardio-arthritis</i>	36
— <i>coli gracilis</i>	39
— <i>equisimilis</i>	35
— <i>erysipelatos</i>	34
— <i>evolutus</i>	45
— <i>faecalis</i>	38
— <i>foetidus</i>	41
— <i>gracilis</i>	39
— <i>intermedius</i>	44
— <i>liquefaciens</i>	39
— <i>longus haemolyticus</i>	34
— <i>longus pathogenes seu erysipelatos</i>	34
— <i>melitensis</i>	88
— <i>micro</i>	43
— <i>mitior</i>	37
— <i>mitis</i>	37
— <i>ovalis</i>	38
— <i>pneumoniae</i>	30
— <i>proteiformis</i>	38
— <i>puerperalis</i>	34
— <i>putridus</i>	42
— <i>putrificus</i>	42
— <i>pyogenes</i>	34
— <i>pyogenes var. scarlatinae</i>	34
— <i>salivarius</i>	36
— <i>scarlatinae</i>	34
— <i>viridans</i>	37
Streptococcus	34
<i>Streptomyces africanus</i>	137
— <i>beddardii</i>	144
— <i>fordii</i>	136
— <i>gallicus</i>	138
— <i>gibsonii</i>	143
— <i>hortonensis</i>	142
— <i>kimberi</i>	145
— <i>listeri</i>	140
— <i>pelletieri</i>	139
— <i>somaliensis</i>	146
— <i>upcottii</i>	141
— <i>willmorei</i>	147
<i>Streptothrix actinomycotica</i>	134
— <i>asteroides</i>	130
— <i>bovis</i>	134
— <i>bovis communis</i>	134
— <i>erysipeloides</i>	52
— <i>israeli</i>	135
— <i>madurae</i>	132
— <i>ratti</i>	100
— <i>rosenbachii</i>	52
— <i>somaliensis</i>	146
<i>Strongyloides stercoralis</i>	267
<i>Strongyloplasma hominis</i>	191
— <i>variola</i>	185
Swamp fever	165-167
Swineherd's disease	165-167
Syphilis	159
<i>Syngospora negronii</i>	280
— <i>robini</i>	280
<i>Syzgiococcus scarlatinae</i>	29

178

Index of Pathogenic Organisms (Bacteria, Protozoa, Worms)
and Infectious Diseases (concluded)

The *italic numbers* in this index are reference numbers corresponding to the *italic numbers* in column 2 of the tables on pages 129–168. Further information on any pathogenic organism (synonyms, characteristics, vectors, diseases, susceptibility to antibiotics, etc.) or infectious disease listed may therefore readily be found by looking under the appropriate number in column 2 of the tables.

T

Tabardillo	169
<i>Taenia aegyptiaca</i>	263
— <i>cucumerina</i>	262
— <i>echinococcus</i>	266
— <i>elliptica</i>	262
— <i>mediocanellata</i>	265
— <i>nana</i>	263
— <i>saginata</i>	265
— <i>solium</i>	264
<i>Taeniorhynchus saginatus</i>	265
Tapeworms	260–266
— armed	264
— beef	265
— broad	260
— dog	266
— dwarf	263
— fat	265
— fish	260
— hydatid	266
— measly	264
— pork	264
— unarmed	265
<i>Tarpeia alpha (beta)</i>	211
— <i>premens</i>	212
Teeth, infections	36, 38
Ténia à épine	260
Tertian benigna (malaria)	242
Tertian maligna (malaria)	244
Tetanus	123
<i>Tetracoccus anaerobius</i>	13
— <i>septicus</i>	12
Tétragène	12
— anaérobie	13
<i>Tetramitus mesnili</i>	239
<i>Theileria tsutsugamushi</i>	172
<i>Thermobacterium intestinale</i>	46
Three-day fever	201
Thrush	280
Tibial fever	165–167, 173
Tick fever	149
<i>Tissierellus parapatrificus</i>	120
Tobia fever	170
Tollwut (rabies)	204
Tonga	160
Tonsillitis	5, 10, 11, 33–35
Tonsils, infections	10, 36
<i>Tortor furens spec. nov.</i>	208
<i>Toxoplasma</i>	241
Trachoma	103, 176
Trench fever	173
<i>Treponema calligrum</i>	162
— <i>carateum</i>	164
— <i>carteri</i>	152
— <i>duttoni</i>	149
— <i>genitalis</i>	163
— <i>hebdomadis</i>	166
— <i>herrejonii</i>	164
— <i>icterogenes</i>	165
— <i>japonicum</i>	4
— <i>kochi</i>	150
— <i>laverani</i>	4
— <i>minor</i>	4
— <i>minutum</i>	163
— <i>morsus muris</i>	4
— <i>mucosum</i>	161
— <i>nodosum</i>	165
— <i>novyi</i>	151
— <i>obermeieri</i>	148
— <i>pallidulum</i>	160
— <i>pallidum</i>	159
— <i>pertenue</i>	160
— <i>pictor</i>	164
— <i>pintae</i>	164
— <i>recurrentis</i>	148
— <i>refringens</i>	154
— <i>rossi</i>	150
— <i>schaudinni</i>	153
— <i>sodoku</i>	4
— <i>venezuelensis</i>	158
— <i>vincenti</i>	153
Tréponème du pian	160
<i>Treponemella muris</i>	4
<i>Tricomonas intestinalis</i>	228
Trichina worm	274
<i>Trichina spiralis</i> , <i>Trichinella spiralis</i>	274
Trichinosis	274
<i>Trichocephalus crenatus</i>	273
— <i>dispar</i>	273

T

<i>Trichocephalus suis</i>	273
— <i>trichiurus</i>	273
<i>Trichomonas buccalis</i>	238
— <i>elongata</i>	238
— <i>hominis</i>	236
— <i>intestinalis</i>	236
— <i>tenax</i>	238
— <i>vaginalis</i>	237
<i>Trichuris trichiura</i>	273
<i>Trifur equorum</i>	213
Trismus	123
Tropica (malaria)	244
<i>Trypanosoma castellani</i>	229
— <i>cruzi</i>	231
— <i>escomeli</i>	231
— <i>fordi</i>	229
— <i>gambiense</i>	229
— <i>hominis</i>	229
— <i>lanfranchii</i>	229
— <i>luis</i>	159
— <i>neotomae</i>	231
— <i>neprevi</i>	229
— <i>rhési</i>	231
— <i>rhodesiense</i>	230
— <i>ugandense</i>	229
— <i>vickersae</i>	231
Tsutsugamushi disease	172
Tuberculosis	34, 35, 128
— bovine	128
Tularaemia	84
Tumours, malignant	256–258
Typhoid fever (<i>Salmonella</i>)	72
Typhus (German). See Typhoid fever	
Typhus fever (<i>Rickettsia</i>)	168–172
— benign	169
— classical	168
— endemic	169
— epidemic	168
— European	168
— exanthematous	168
— Minas Gerais	170
— murine	169
— São Paulo	170
— scrub	172
— Shimamushi mite-borne	172

U

<i>Uncinaria americana</i>	277
— <i>duodenalis</i>	275
Undulant fever	88–90
Urogenital system, infections	1, 54, 55, 61–63, 80, 92, 93
— inflammation	24, 256–258
Urticaria	272
Uta	235

V

<i>Vaccinia</i>	185
<i>Vaccinia bovis</i>	185
Vaginitis	106–108
<i>Vallorillus fallax</i>	110
Varicella	186
Variola major	185
— minor	185
<i>Veillonella alcalescens</i>	26
— <i>alcalescens</i> var. <i>gingivalis</i>	27
— <i>alcalescens</i> var. <i>minutissima</i>	28
— <i>alcalescens</i> var. <i>syzygios</i>	29
— <i>gazogenes</i>	26
— <i>gazogenes</i> var. <i>gingivalis</i>	27
— <i>gazogenes</i> var. <i>minutissima</i>	28
— <i>gazogenes</i> var. <i>syzygios</i>	29
— <i>parvula</i>	25
Ver de Guinée	272
— lombricoïde	278
— solitaire	264
Verrucae	190
Verruga peruana	175
Vibrio, cholera	2
— El Tor	2
<i>Vibrio alcaligenes</i>	53
— <i>cholerae asiaticae</i>	2
— <i>comma</i>	2
— <i>finkleri</i>	3

V

<i>Vibrio pasteurii</i>	111
— <i>proteus</i>	3
— <i>septicus</i>	111
— <i>typhosus</i>	72
Vibrio septique	111
Virales (viruses)	185–218
Virus of A-encephalitis	195
— of B-encephalitis	196
— of C-encephalitis	198
— cat-scratch	216
— chickenpox	186
— common cold	212
— cowpox	185
— Coxsackie group	201
— dengue	206
— of encephalitis	192, 193, 195–198
— of epidemic haemorrhagic fever	217
— of equine encephalomyelitis	199
— of equine infectious anaemia	213
— de la fièvre aphteuse	209
— of foot and mouth disease	209
— grippal	211
— hepatitis	214, 215
— of herpes febrilis	189
— of herpes simplex	189
— of herpes zoster	187
— of infective hepatitis	214
— influenza	211
— of lymphocytic choriomeningitis	202
— of lymphocytic pseudochoriomeningitis	203
— of Manchurian fever	217
— measles	188
— of molluscum contagiosum	191
— mumps	218
— of Newcastle disease	208
— papillomateux	190
— of pappataci fever	210
— poliomyelitis	200
— rabies	204
— of Rift Valley fever	207
— rougeoleux	188
— of serum hepatitis	215
— smallpox	185
— varicella	186
— variola	185
— warts	190
— of X-disease	194
— yellow-fever	205
Volhynia fever	173

W

Warts	190
Water fever	165–167
WATERHOUSE-FRIEDRICHSEN syndrome	16
WEIL's disease	165–167
<i>Weinbergillus histolyticus</i>	126
<i>Welchia perfringens</i>	117
<i>Welchillia aerogenes</i>	117
Whipworm	273
White mouth	280
Whitlows	5
Whooping cough	98
Windpocken (chickenpox)	186
Wounds, infections	1, 34, 40, 42, 110–122, 126, 127
<i>Wuchereria bancrofti</i> , <i>Wuchereria bancrofti</i>	268
— <i>malayi</i>	269

X

X-Disease	194
-----------	-----

Y

Yaws	160
Yellow fever	205
<i>Yokogawa yokogawai</i>	249

Z

Zona	187
Zwergbandwurm	263
<i>Zymosarcina ventriculi</i>	14

(and of the placenta)

Gonadotropic hormones

Chemistry. Glycoproteins with hexosamine and carbohydrate. Mol. wt. 60,000 to 100,000, water-soluble²¹.

Unit. International units: gonadotropic hormones of serum = activity of 0.25 mg of the international standard preparation; gonadotropic hormones of the placenta = activity of 0.1 mg of the international standard preparation. The rat or mouse unit corresponds to the minimum quantity which in 50% of the experimental animals (immature rats or mice) produces a macroscopically visible reaction in the ovaries (corpora lutea or haemorrhage).

Methods of assay¹

At commencement of and during pregnancy (pregnancy tests):

FRIEDMAN test^{2,3}: 2 injections each of 10 ml of the urine under test, with a 24-hour interval, in the aural veins of the female rabbit. Positive, if haemorrhagic follicles or blood spots are observed 48 hours after the second injection.

Rat tests (modifications of the original ASCHHEIM-ZONDEK test on mice): positive, if subcutaneous or intraperitoneal injection of the test urine in young female rats produces hyperaemia of the ovaries after 24 hours⁴, 6 hours^{5,6}, or 2 hours^{7,8}.

Frog tests: with male frogs⁹, according to country: *Rana pipiens*¹⁰⁻¹⁶, *Rana esculenta*¹⁷: positive, if an injection of the test serum or urine in the dorsal lymph sac provokes ejaculation in 2-3 hours.

Toad tests: *Xenopus laevis*^{18,19}; positive, if an injection of the test liquid provokes ovulation after 8-12 hours.

Other than in pregnancy:

The same tests as during pregnancy can be used except that the test urine or serum must first be fractionated in order to increase the concentration of the gonadotropic hormones. This is achieved by precipitation of the proteins from the acidified sample by ethyl alcohol, followed by extraction of the hormones with ether or acetone.

Function^{20,21,23}

The structure, function and internal secretion of the gonads of both sexes are completely dependent on the trophic action of the hormones of the anterior pituitary, the gonadotropic hormones. Hypophysectomy results in rapid and extensive atrophy of the gonads: (ovaries) the follicles only partly develop and then degenerate; the ova are no longer capable of fertilization; the corpora lutea become atrophied and, since ovulation no longer takes place, are not regenerated; the interstitial tissue atrophies; the secretion of oestrogens (follicles) and progesterone (corpora lutea) ceases. (Testes) The generative and interstitial tissues become atrophied and degenerate, the formation of testosterone (interstitial tissue) ceases. These degenerative changes, as a result of the non-production of sex hormones, have a corresponding effect on the secondary sexual characters; the extent of this depends very largely on the time at which the production of gonadotropins ceases or begins to diminish.

The gonads are influenced by two hormones, both of which can be prepared in pure form: the follicle-stimulating hormone²³⁻²⁶ and the luteinizing hormone^{27,28}.

The *follicle-stimulating hormone* (FSH) stimulates in women the development of the follicles, the ripening of the ova, and in conjunction with traces of the luteinizing hormone, the secretion of oestrogens by the follicles. In men it stimulates the generative tissue of the testes and thereby the formation of spermatozoa.

The *luteinizing hormone* (LH) is responsible for ovulation and, in conjunction with the lactogenic hormone, for the formation and development of the corpora lutea and thus for the secretion of progesterone. In men it stimulates the interstitial tissue and thus the secretion of testosterone.

Sites of formation

FSH is produced by the basophil cells, LH by the acidophil-carminophil²⁹ cells³⁰ of the anterior pituitary (see also Lactogenic hormone, page 180).

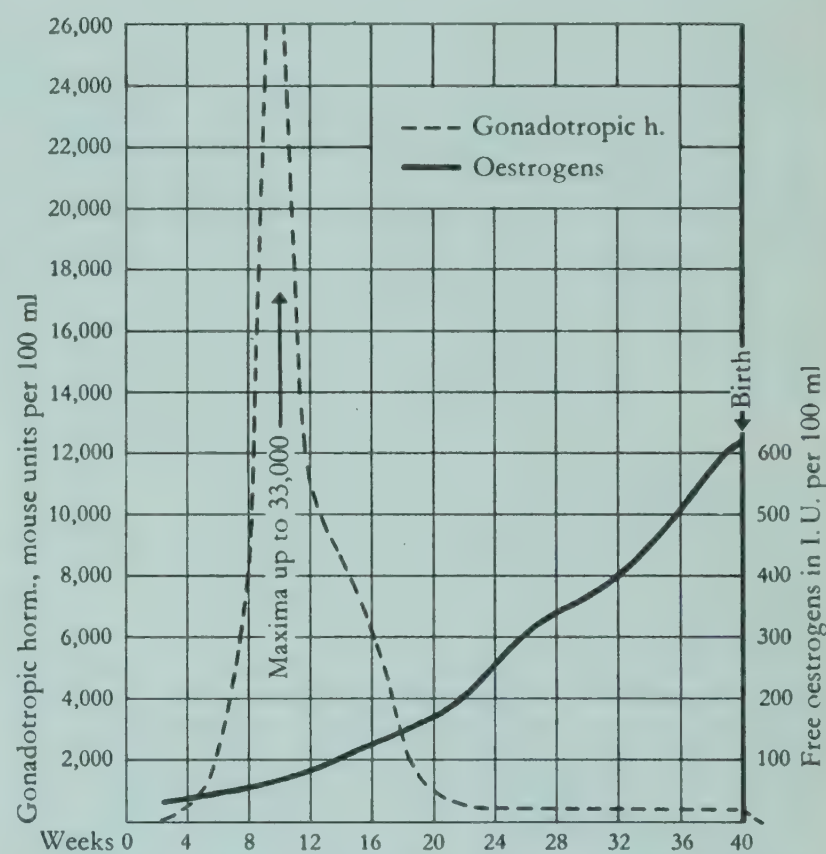
During pregnancy the placenta produces a considerable quantity of gonadotropic hormones differing, however, both quantitatively and qualitatively from those of the pituitary: in the latter the FSH-activity predominates, in the former the LH-activity; the activity of the pituitary hormones is similar in all animal species, in contrast to that of the hormones of the placenta; the gonadotropic hormones of the placenta never cause, for example, ovulation or luteinization in women²².

Urinary elimination. The gonadotropic hormones of men and the anthropoids are eliminated in the urine, in contrast to those of all other mammals.

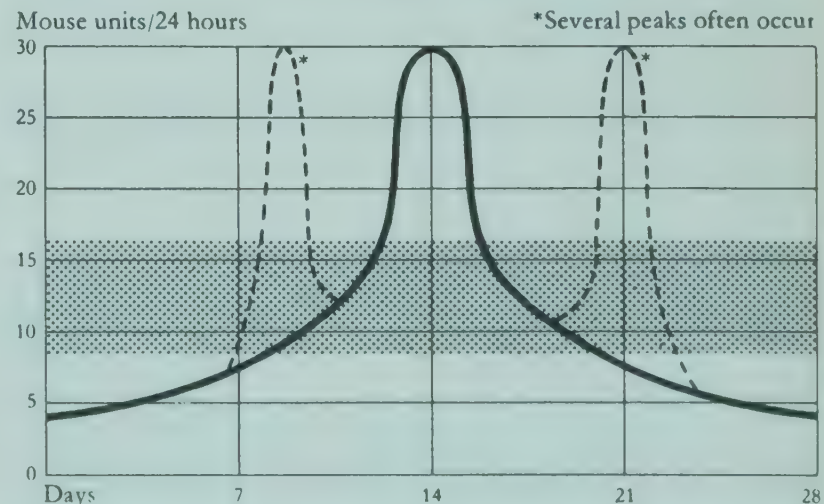
Regulation of the gonadotropin secretion

Although the exact mechanism of the regulation of the secretion is unknown the following has been established:

Basal secretion. In men this is constant, in women it is dependent on the cyclic changes, with a maximum at the time of ovulation



Gonadotropic hormones and oestrogens in the blood of pregnant women. After CANTAROW and TRUMPER, *Clinical Biochemistry*, Philadelphia, 1945.



Elimination of gonadotropic hormones in urine of men (shaded area) and of women in the course of the menstrual cycle (curve with one or more peaks). After RAKOFF, A. E., *Med. Clin. N. Amer.*, **26**, 1915, 1942.

(several maxima often occur). The quantity of gonadotropins secreted is inversely proportional to the quantity of sex hormones secreted, i.e. an increase in the output of sex hormones is accompanied by a decrease in the output of the gonadotropic hormones of the pituitary, and vice versa. For this reason, for example, very high titres of gonadotropins are found in castrated men. This

Gonadotropic hormones (continued)

interdependence has a clinical application, in that the gonadotropin secretion of the pituitary and thereby, as a secondary effect, the gametogenesis, can be inhibited by administration of large quantities of sex hormones.

The constant or cyclic basal secretion is capable of being modified by both psychic and sensory influences. In rats, for example, these influences are transmitted to the anterior pituitary via the hypothalamus, most probably by means of adrenergic substances^{31,32} (they can be blocked in a first phase by anticholinergic substances [atropine], in a second phase by noradrenaline-blocking substances). The central regulation of gonadotropin secretion can also be influenced by barbiturate "twilight sleep", as has already been observed³³ in man.

Pituitary interrelations between the various hormonal systems. The nature of these has not yet been elucidated, although it has been shown that in stress or in non-functioning of the thyroid (i.e. with overproduction of adrenocorticotrophic or thyrotrophic hormone respectively) the secretion of gonadotropins is lowered. Hyperactivity of the thyroid can similarly result in paralysis of gonadotropin secretion.

Diagnostic significance

The methods of assay of gonadotropins can be applied to the differential diagnosis of early pregnancy, incipient miscarriage during the first 4 weeks of pregnancy, cystic mole, chorio-epithelioma (uterus, ovaries, testes, metastases).

Therapeutic application

The *gonadotropic hormones of the placenta* (extracted from the urine of pregnant women or from the serum of pregnant mares) have no application in medicine. *Gonadotropic hormones of the pituitary:* (women) anovulatory cycles, menometrorrhagia, amenorrhoea, hypogonadism; (men) oligospermia³⁴, eunuchoidism, cryptorchidism.

Contraindication: diabetes mellitus.

(It must be emphasized that after hypophysectomy the response of the atrophied gonads to gonadotropins is the less, the longer the elapsed time between the hypophysectomy and the exogenous administration. Completely atrophied gonads can apparently no longer be reversibly influenced.)

¹⁾ For a review see GREENBLATT, R. B., *J. clin. Endocr.*, **4**, 410, 1944. ²⁾ FRIEDMAN and LAPHAM, *Amer. J. Obstet. Gynec.*, **21**, 3405, 1931. ³⁾ KELLY and WOODS, *J. Amer. med. Ass.*, **108**, 615, 1937. ⁴⁾ KELSO, R. E., *Amer. J. clin. Path.*, **10**, 293, 1940. ⁵⁾ SALMON et al., *J. clin. Endocr.*, **2**, 167, 1942. ⁶⁾ KLINE, B. *Scientific Exhibit. A.M.A.*, Chicago, 1944. ⁷⁾ SALMON et al., *Endocrinology*, **30**, Supplement, 1039, 1942. ⁸⁾ KUPPERMANN et al., *J. clin. Endocr.*, **3**, 548, 1943. ⁹⁾ GALLI-MAININI, C., *J. clin. Endocr.*, **7**, 653, 1947. ¹⁰⁾ WILTBERGER and MILLER, *Science*, **107**, 198, 1948. ¹¹⁾ HASKINS and SHERMAN, *Endocrinology*, **44**, 542, 1949. ¹²⁾ BRODY, H., *Amer. J. Obstet. Gynec.*, **57**, 558, 1949. ¹³⁾ MAIER, E. C., *West. J. Surg.*, **57**, 558, 1949. ¹⁴⁾ GARDNER and HARRIS, *Amer. J. Obstet. Gynec.*, **59**, 350, 1950. ¹⁵⁾ GREENBLATT et al., *J. clin. Endocr.*, **10**, 265, 1950. ¹⁶⁾ GREENBLATT et al., *Fertility*, **1**, 533, 1950. ¹⁷⁾ JAUBERT et al., *Concours méd.*, **74**, 377, 1952. ¹⁸⁾ SHAPIRO and ZWARENSTEIN, *S. Afr. med. J.*, **9**, 202, 1935. ¹⁹⁾ WEISMANN and COATES, *West. J. Surg.*, **52**, 121, 1944. ²⁰⁾ HOUSSAY et al., *Physiologie Humaine*, Paris, 1950. ²¹⁾ VON BUDDENBROCK, W., *Hormone, Vergleichende Physiologie*, Vol. IV, Basle, 1950. ²²⁾ GREENBLATT, R. B., *Office Endocrinology*, Springfield, 1952. ²³⁾ FRAENKEL-CONRAT et al., *Ann. de la Faculté de Médecine*, Montevideo, **25**, 1940. ²⁴⁾ GREEP et al., *J. biol. Chem.*, **133**, 289, 1940. ²⁵⁾ McCULLACH and BOWMAN, *Endocrinology*, **26**, 999, 1940. ²⁶⁾ CHOW, F., *Ann. N. Y. Acad. Sci.*, **43**, 309, 1943. ²⁷⁾ FEWOLD et al., *Endocrinology*, **26**, 999, 1940. ²⁸⁾ FEWOLD, H. L., *Ann. N. Y. Acad. Sci.*, **43**, 321, 1943. ²⁹⁾ DAWSON and FRIEDGOOD, *Stain Technology*, 1938. ³⁰⁾ DAWSON, A. B., *Amer. J. Anat.*, **78**, 347, 1946. ³¹⁾ MARKEE et al., *Recent Progr. Hormone Res.*, **7**, 139, 1952. ³²⁾ SAWYER, C. H., *ibid.*, **7**, 161, 1952. ³³⁾ WESTMAN, A., *ibid.*, **7**, 160, 1952. ³⁴⁾ See also GASSNER, X. F., *ibid.*, **7**, 200, 1952.

Lactogenic hormone

(prolactin, mammatropin, luteotropin)

Chemistry

Protein, insoluble in water, unstable to boiling, decomposed by trypsin and pepsin. Mol. wt. 32,000–35,000, isoelectric point pH 5.65¹. Chemical constitution²: 15.86% nitrogen; 1.79% sulphur; 1% amino-nitrogen; 8.6% arginine; 11.6% aspartic acid; 3.1% cystine; 14.1% glutamic acid; 4.0% glycine; 4.5% histidine; 7.2% isoleucine; 12.5% leucine; 5.3% lysine; 3.6% methionine; 4.1% phenylalanine; 6.2% proline; 6.5% serine; 4.8% threonine; 1.2% tryptophan; 4.7% tyrosine; 5.9% valine.

Unit. International unit = 0.1 mg of the international standard preparation (UNO 1950).

Methods of test and assay

Proliferation test on the crops of young pigeons (RIDDLE and BATES³). For other tests see ^{4,5} and ⁶.

Physiology and function

Prolactin, discovered in 1928 by STRICKER and GRÜTER⁷, is so widely distributed in all warm-blooded animals and affects in different species such widely different organs, that the name "prolactin" or lactogenic hormone is undoubtedly too restrictive. The lactogenic hormone is formed in the carminophil cells of the anterior lobe (the carminophil cells are acidophil cells⁸ which in coitus are stimulated to increased degranulation and thus to increased secretion of hormones⁹). Prolactin is found both in men and women up to an advanced age¹⁰. The prolactin content of the pituitary under normal conditions is the same in both sexes; during pregnancy the titre increases at first slowly, then more rapidly.

Prolactin is luteotropic¹¹ (see also gonadotropic hormones). In its absence the corpora lutea are incapable of secreting progesterone¹⁰. Prolactin inhibits the action of the follicular hormones, is responsible for maternal behaviour in the female (probably a secondary effect of the progesterone stimulation through the luteotropic component of the lactogenic hormone) and has a

marked effect, not yet explained (direct or indirect) on cellular metabolism¹⁰. The lactogenic hormone appears to be essential for the growth of the mammary glands and for lactogenesis and galactopoiesis.

Physiology of the mammary glands

Growth. The lactogenic hormone, in combination with oestrogens (primarily) and progesterone, has a direct growth-promoting action on the mammary gland tissue^{12–15}. Prolactin here appears to sensitize the mammary glands to the growth-promoting effect of the female sex hormones, especially of the oestrogens¹⁶. This supposition is based on the growth-promoting effect of steroid hormones on the mammary glands of hypophysectomized animals¹⁷. Normal functioning of the adrenal cortex¹⁸ and the thyroid^{19–23} is also necessary for normal growth of the mammary glands, although these organs, or rather their hormones, have no direct effect on the growth.

The development of the mammary glands is also stimulated by suckling^{16,24}, from which the existence of a neurohumoral reflex arc mammary gland–hypothalamus–anterior pituitary–mammary gland must be assumed. This reflex arc is not indispensable, since mammary gland grafts, in which such an arc does not exist, develop normally given normal endocrine function²⁵.

Lactogenesis. Prolactin in combination with adrenal hormones^{26,27} and others of uncertain significance is essential to lactogenesis.

Galactopoiesis (maintenance of the lactic secretion). Prolactin itself is not capable of maintaining or increasing lactation^{28–31}, in contrast to total pituitary extracts. Here it appears that the growth hormone plays an important part the nature of which is not yet understood³².

Ejection of the lactic secretion. In the breasts about 50% of the milk is located in the alveoli and the fine-calibre ducts³³, from which it is expressed, and thus made available to the child, by the effect of contractile tissue stimulated during suckling. The existence of such fibres, part of the smooth musculature, has in fact recently been demonstrated^{34,35}. Stimulations which cause contraction of these fibres are tactile stimulations of the uterine cervix³⁶ (suckling on the other hand causes uterine contractions), stimulation of the central vagus³⁷, and the suckling stimulus^{33,38}.

Lactogenic hormone (continued)

On these grounds the existence of a neurohumoral reflex arc for the development of the breasts must be assumed. It is highly probably that oxytocin is a link in this reflex arc, since doses of even several thousandths of a unit cause milk ejection^{18,37,39}. That it is a question of a neurohumoral and not a purely nervous reflex has been shown by the fact that a surviving isolated bovine udder ejected milk when it was perfused with blood from a cow bled just after application of the milking stimulus^{40,41}. It has also been shown that in the water-loaded cow suckling causes an anti-diuretic response of pituitary type^{42,43,44}, that is to say, that the posterior pituitary is activated by the suckling. The antidiuretic principle cannot, however, be the cause of the ejection of milk, since administration of posterior lobe extracts possessing this antidiuretic action does not lead to ejection.

Therapeutic application

Development of the breasts. Moderate parenteral or local doses of oestrogens have the most favourable effect (+ massage). Where inadequate functioning of other endocrine glands is indicated, appropriate therapy.

Lactation. Promotion of lactation by means of hormones is hardly yet possible. The most effective means of maintaining and increasing lactation are continuous and intensive sucking of the breast nipples, the complete emptying of the glands, and the psychic readiness of the mother to satisfy her child.

The lactogenic hormone has been shown to be ineffective in promoting either development of the breasts or lactic secretion¹⁷.

Large doses of oestrogens retard lactation and are well tolerated after parturition.

¹) WHITE, A., *Ann. N. Y. Acad. Sci.*, **43**, 363, 1943. ²) LI, V. H., *J. biol. Chem.*, **178**, 459, 1949. ³) RIDDLE et al., *Amer. J. Physiol.*, **105**, 191, 1933. ⁴) BATES, R. W., *Cold Spr. Harb. Symp. quant. Biol.*, **5**, 191, 1937. ⁵) LYONS, W. R., *ibid.*, **5**, 198, 1937. ⁶) RIDDLE and BATES, in ALLEN, E., *Sex and Internal Secretions*, 2nd ed., Baltimore, 1088, 1939. ⁷) STRICKER and GRÜTER, *C. R. Soc. Biol.*, **99**, 1978, 1928. ⁸) DAWSON and FRIEDGOOD, *Stain Technology*, 1938. ⁹) DAWSON, A. B., *J. Anat.*, **78**, 347, 1946. ¹⁰) VON BUDDENBROCK, W., *Hormone, Vergleichende Physiologie*, Vol. IV, Basle, 1950. ¹¹) EVANS et al., *Endocrinology*, **28**, 933, 1941. ¹²) GARDNER and WHITE, *Proc. Soc. exp. Biol.*, **48**, 590, 1941. ¹³) LYONS, W. R., *ibid.*, **51**, 308, 1942. ¹⁴) REECE and LEATHEM, *ibid.*, **59**, 122, 1945. ¹⁵) MEITES and TURNER, *Missouri Agr. exp. Sta. Res. Bull.*, No. 415, 1948. ¹⁶) FOLLEY, S. J., *Recent Progr. Hormone Res.*, **7**, 107, 1952. ¹⁷) For a review see FOLLEY and MALPRESS, in PINCUS, *The Hormones*, Vol. 1, New York, 1948. ¹⁸) TRENTIN and TURNER, *Missouri Agr. exp. Sta. Res. Bull.*, No. 418, 1948. ¹⁹) WEICHERT and BOYD, *Anat. Rec.*, **59**, 157, 1934. ²⁰) CHAMORRO, A., *Ann. Endocr.*, **9**, 350, 1948. ²¹) CHAMORRO, A., *C. R. Soc. Biol.*, **142**, 426, 1948. ²²) DESCLIN, L., *C. R. Soc. Biol.*, **142**, 1575, 1948. ²³) JOHNSTON and SMITHCORS, *Endocrinology*, **43**, 193, 1948. ²⁴) SELYE and MCKEOWN, *Proc. Soc. exp. Biol.*, **31**, 683, 1934. ²⁵) STRICKER, P., *C. R. Soc. Biol.*, **102**, 1076, 1929. ²⁶) NELSON et al., *Endocrinology*, **33**, 325, 1943. ²⁷) REECE, R. P., *Proc. Soc. exp. Biol.*, **40**, 25, 1939. ²⁸) FOLLEY and YOUNG, *Proc. roy. Soc. B*, **126**, 45, 1938. ²⁹) FOLLEY and YOUNG, *Biochem. J.*, **33**, 192, 1939. ³⁰) FOLLEY and YOUNG, *J. Endocr.*, **2**, 226, 1940. ³¹) FOLLEY and YOUNG, *Lancet*, **1**, 380, 1941. ³²) COTES et al., *Nature*, **164**, 992, 1949. ³³) FOLLEY and GREENBAUM, *Biochem. J.*, **41**, 261, 1947. ³⁴) RICHARDSON, K. C., *Proc. roy. Soc. B*, **136**, 30, 1949. ³⁵) LINZELL, J. L., *J. Anat.*, **86**, 49, 1952. ³⁶) ANDERSSON, B., *Acta physiol. scand.*, **23**, 1, 1951. ³⁷) ANDERSSON, B., *ibid.*, **23**, 24, 1951. ³⁸) SELYE, H., *Amer. J. Physiol.*, **107**, 535, 1934. ³⁹) CROSS and HARRIS, *J. Physiol.*, **113**, 35 P, 1951. ⁴⁰) PETERSEN and LUDWICK, *Fed. Proc.*, **1**, 66, 1942. ⁴¹) PEETERS et al., *Arch. int. Pharmacodyn.*, **75**, 85, 1947. ⁴²) PEETERS et al., *ibid.*, **80**, 355, 1949. ⁴³) PEETERS et al., *ibid.*, **84**, 209, 1950. ⁴⁴) CROSS, B. A., *Nature*, **166**, 612, 1950.

Thyrotropic hormone (thyrotropin)

Chemistry. Protein of relatively low mol. wt. Slightly soluble in water, dilute acids and alkalis, insoluble in ether, alcohol and chloroform. Stable indefinitely in the dry state, unstable in aqueous solution and when heated.

Unit. No international unit.

Methods of test and assay. Histological and weight control of thyroid activation in guinea pigs (JUNKMANN-SCHÖLLER).

Physiology and function

Formed by the basophil cells of the anterior lobe. Production (in the male ca. 100% greater) increases rapidly with growth and in pregnancy (increase ca. 40% at termination of pregnancy).

After intravenous injection the hormone disappears rapidly from the blood (complete disappearance after 60 min.).

Functions:

1. Maintenance of functioning of the thyroid (non-functioning of the pituitary causes atrophy of the thyroid).
2. Stimulation of the hormonal output of the thyroid.
3. Stimulation of the hormonal distribution from the thyroid into the blood (administration of thyrotropic hormone reduces the iodine content of the thyroid).

The formation and distribution of the thyrotropic hormone is regulated antagonistically by the iodine level of the blood (iodine level = inorganic iodine, thyroxine, diiodotyrosine). Absence of the thyrotropic hormone results in atrophy of the thyroid and accumulation of colloids, thyroidectomy on the other hand causes hypertrophy of the anterior lobe and specific changes in the basophil cells (thyroidectomy cells).

Therapeutic application. As for thyroxine, provided that the thyroid tissue is intact.

Indefinite glandotropic hormones

The existence of hormones with specific activity towards parathyroids, pancreas and adrenal medulla is much in dispute. Hypophysectomy results often, but not always, in atrophic changes in these organs which can be reversed by the administration of pituitary extracts. It is doubtful, however, if this substitutive action can be attributed to specific pituitary hormones, since similar effects can be obtained with highly purified preparations such as prolactin.

Indefinite hormones of metabolism

The diabetogenic principle (HOUSSAY and BIASOTTI)

The severe diabetes which results from pancreatectomy does not occur, or occurs only in mild form, when the anterior pituitary is simultaneously removed. HOUSSAY and POTICK (1929) showed that in the toad hypophysectomy markedly increased the sensitivity to insulin, that administration of anterior pituitary extracts to normal or hypophysectomized animals reduced the sensitivity to insulin, and that protracted treatment of normal animals with anterior pituitary extracts resulted in a condition resembling diabetes: the "diabetogenic principle". Later HOUSSAY found a lowering of insulin elimination in dogs rendered diabetic by injection of anterior pituitary extracts, and YOUNG (1938) established by histological studies that the LANGERHANS islets showed changes which suffice to explain the onset of diabetes. Since the removal of the adrenals also alleviates pancreatic diabetes, it is likely that two pituitary hormones are involved in the diabetogenic principle, one acting directly and the other via the adrenal cortex (cf. Growth hormone, page 192, and Corticotropin, pages 182-189).

The hormone of carbohydrate metabolism

(ANSELMINO and HOFFMANN, 1935; COLLIP, 1935)

The anterior lobe contains a substance which in the space of 1-3 hours lowers the liver glycogen by 90%, followed by an increase in the blood sugar of relatively long duration. In the healthy body this substance is present in the blood only after a carbohydrate meal, in fasting it is lacking. It also lowers the liver fatty acids, and has been found in higher concentrations in diabetics.

The contra-insular principle (LUCKE and KRÖGER, 1936)

This substance, like ANSELMINO's hormone of carbohydrate metabolism, also raises the blood-sugar level, but the effect is of much shorter duration. According to LUCKE it is secreted in the cerebrospinal fluid and acts through a centre in the central nervous system which activates the adrenal medulla. LUCKE's principle is possibly identical with HOUSSAY's diabetogenic principle.

The following should also be mentioned: the **glycotropic factor** of MARKS, YOUNG, et al.; the **ketogenic principle** of BURN and LING (1930), which is probably closely linked with the secondary effects of the regulation of protein metabolism by the growth hormone (see page 192).

Corticotropin (Adrenocorticotrophic hormone, ACTH)

Bibliography: see pages 190 and 191.

1. Chemistry

ACTH, like insulin, was formerly thought to be a hormone-protein combination, and the preparations currently obtainable usually consist in fact of protein extracts from the pituitaries of pigs, sheep, whales, etc. The active principle of these preparations has now been shown to consist of a polypeptide built up of amino-acids in a straight chain, the structure varying according to the animal by which it is produced. Thus from sheep pituitary LI et al.^{1,2} have isolated and purified α -corticotropin, containing 39 amino-acid units and resembling β -corticotropin, isolated by BELL³ from pig pituitary and also containing 39 amino-acid units but in a different order. In addition the ARMOUR⁴ and MERCK⁵ research groups have isolated respectively corticotropin-A from unhydrolyzed pig pituitary and corticotropin-B from the pepsin-hydrolyzed glands. Both are highly-active compounds differing in structure from α - and β -corticotropins.

2. Unit

1 international unit = activity of 1 mg of the international standard preparation = activity of 1 mg of the ARMOUR preparation La-1-A prepared in 1944 by MUNSON et al.⁶. (Activity measured by ascorbic acid test of SAYERS et al.⁷)

3. Methods of test and assay

ACTH. The quickest and most sensitive test is the ascorbic acid test of SAYERS et al.⁷ on hypophysectomized rats. Stimulation of hormonal output by ACTH results in a lowering of the ascorbic acid content of the adrenal cortex. The latter is measured a certain time after injection of the ACTH sample and compared with the content in control animals. This test appears to be specific, although increased secretion of adrenocortical hormones has been observed in scorbutic guinea pigs injected with ACTH⁸.

The activities of ACTH preparations determined by the ascorbic acid test correspond closely with their therapeutic activities^{2,9}, particularly with relation to the eosinophil depression^{10,11}, lymphopenia, and the increase in liver glycogen¹².

Corticosteroids*. An indirect method of assay, suitable for clinical purposes, is the rapid and highly sensitive eosinophil test of SPIERS et al.¹³ on adrenalectomized mice kept alive by means of implanted cortexone (deoxycorticosterone) tablets. An adrenaline injection is followed 4 hours later by an injection of the sample under test for 11-17-O-corticosteroids; counts of eosinophils are made immediately prior to this injection and 3 hours after. The percentage reduction in the count corresponds to the quantity of corticosteroids in the sample. This method has the advantage that untreated urine (without prior concentration of the corticosteroids) may be used. It gives higher values than the usual biological methods since losses of corticosteroids during the prior concentration are avoided.

Determination of the so-called "formaldehydogenic" steroid fraction of urine (HOLLANDER et al.¹⁴, as modified by HENLY and POTTER¹⁵): in clinical studies this fraction and the corticosteroid fraction have been considered as identical, an assumption which more recent work has shown must be accepted with caution.

Direct chemical-chromatographic methods, which have the advantage of determining not only the steroid spectrum but also individual steroids in the fraction, are those of BURTON et al.¹⁶, BUSH, I. E.¹⁷, HÜBENER et al.¹⁸, NELSON et al.¹⁹, etc.

For a review and discussion of the assay of steroids, see *Recent Progr. Hormone Res.* 9, 1954.

4. Sites of formation

After a long period of uncertainty HERLANT^{20,21} succeeded in 1953 in demonstrating that ACTH is formed in the acidophil cells of the anterior lobe. The placenta also forms substances with ACTH-activity²²⁻²⁴. The recent discovery that some strains of bacteria** produce substances similar to ACTH²⁵ is of particular interest in being the first evidence of the existence of substances similar to pituitary hormones outside the animal kingdom.

5. ACTH in blood and urine

The ACTH concentration in blood and urine is extremely small and can barely be detected by current methods. Concentrations of 59 to 193 milli-units per 100 ml serum have been measured using the ascorbic acid test of SAYERS^{26,27}. Recent researches using the oxycellulose technique of ASTWOOD²⁸ have shown, however, that the ACTH concentration in blood must be less than 0.5 milli-units per 100 ml²⁹.

ACTH administered intravenously in rats disappears completely from the blood in 20 minutes, the half-life being 5 minutes³⁰.

6. Corticosteroids in blood and urine

Blood. The very low titre of 11-17-O-corticosteroids in peripheral venous blood amounts to 4-10 micrograms (mainly hydrocortisone, determined chromatographically)³¹. After intense stimulation³² of the adrenal cortex by 75 mg of ACTH administered intravenously, the titre in peripheral blood barely reaches 10 μ g/100 ml, while at the same time a titre of ca. 38 μ g/100 ml is found in the renal veins. This points to a rapid absorption of corticosteroids out of the blood stream, as does also the rapid drop in concentration from ca. 480 μ g to ca. 50 μ g/100 ml during 30 minutes after an intravenous injection of 200 mg of cortisone³².

Urine. The corticosteroids occur as such in urine, mainly in the form of degradation products in the 17-ketosteroid fraction and to a very small extent in the non-ketosteroid fraction³³. The total of all the steroids in urine identified as metabolites of corticosteroids is only a few per cent of the total quantity secreted by the adrenal cortex³⁴.

The *ketosteroid fraction*³³⁻³⁷ (see also page 200) in adults usually far exceeds the other fractions. In men at least 50% of this fraction consists of metabolites of adrenocortical hormones, while in women and children it consists exclusively of these hormones.

The *corticosteroid fraction* contains a total quantity of ca. 15 to 40 μ g¹⁶ of hydrocortisone and cortisone^{38,39}, as well as other unknown active and inactive corticosteroids, but no cortexone¹⁶. In CUSHING's syndrome⁴⁰ and in ACTH therapy^{41,42} the main steroid of this fraction is hydrocortisone. The total quantity of 11-17-O-corticosteroids, measured by the method of SPIERS et al.¹³, is ca. 3 mg/24 hours. This may increase up to sixfold after ACTH injection¹³ and up to fourfold in strong stress and CUSHING's syndrome⁴³.

The *total titre* of urinary steroids in the above fractions rises and falls with the adrenocortical activity. This is usually also the case for each individual fraction, although the relative amounts of the fractions vary greatly with age and sex. They show marked differences in one and the same person or between different persons according to physiological or pathological differences. There is therefore no strict correlation between the individual fractions^{44,45}. Examples of these variations are given in the table on the next page.

In a number of diseases, particularly cancer, the appearance in the urine of abnormal steroids not existing in the healthy individual has been observed⁴⁶.

The origins of these changes in the spectrum of the urinary steroids are not known with any certainty. They are possibly due to metabolic changes, or to changes in the spectrum of the adrenocortical steroids, or to a combination of both.

From the clinical point of view the following inferences may be drawn: 1. When a quantitative estimate of adrenocortical activity on the basis of urinary steroids is made, the assay of a single fraction has only a relative value; in those cases where one fraction shows abnormal values, the estimate should be based on at least the values of the 17-ketosteroid fraction and of the corticosteroid fraction; 2. A qualitative estimate, based on the steroids eliminated in the urine, of the spectrum of the hormones secreted by the adrenal cortex will be impossible until steroid metabolism under the most diverse conditions has been elucidated; 3. Changes in the urinary steroid spectrum will only have a diagnostic value when sufficient clinical experience has been amassed.

* 11-17-O-Corticosteroids = Hydrocortisone + cortisone. ** Among these is *Bacillus licheniformis*, which produces bacitracin.

Physiological and pathological changes in the relative amounts of the urinary fractions: 17-ketosteroids and 11-17-O-corticosteroids^{36, 37, 45, 47-53}

Growth	17-Ketosteroids	11-17-O-Corticosteroids
Birth to 2nd year	Already present at birth in minimal amount, diminishing from the 1st day, then gradually increasing and reaching at 18 months the level of the 1st-3rd day.	Increase relatively rapid during first two weeks, then slower.
2nd to 5th year	Relatively constant	Regular increase, reaching adult level in the 5th year.
5th year to puberty	Slow increase at first; sharp rise at puberty to adult level . . .	Constant, unaffected by puberty.
Pregnancy	Relatively constant	Increase
Stress	Distinct increase, but less than under ACTH. Increase in titre less than that of corticosteroids. Return to normal level usually two days after a trauma.	Increase much greater than that of ketosteroids. Return to normal level only in convalescence.
ACTH therapy		
Adults	Sharp increase, simultaneous with that of corticosteroids but only half as great. Proportion of β -ketosteroids in the fraction increases.—Increase in ketosteroids under ACTH is variable and dependent on many external and internal factors; e.g. an increase in salt intake can increase the elimination of ketosteroids.	Sharp increase, simultaneous with that of ketosteroids but twice as great.
Children up to 15 years	Variations similar to those for adults. The absolute value for ketosteroids can reach the adult level.	As for adults.
Infants	As for adults, but increase is on the average one sixth of that of corticosteroids.	As for adults, but increase is on the average six times that of ketosteroids.
Adrenogenital syndrome		
Women (inc. pseudo-hermaphroditism)	Usually greatly increased	Normal, or slight increase or decrease.
Hermaphroditism	Normal	Normal.
Men	Usually greatly increased	Normal, or slight increase or decrease.
Hirsutism without other clinical symptoms (men and women)	Normal	Normal.
CUSHING's syndrome	Normal or slight increase, more variable in adrenal than in pituitary CUSHING.	Large increase.
Acromegaly		
active	Increase	Increase.
arrested	Normal	Normal.
ADDISON's disease	Large reduction. In women almost nil, in men somewhat more. Nil value in men usually indicates secondary (pituitary) adrenocortical insufficiency.	Almost nil, can increase slightly under stress.
Hypothyreoses	Reduction (in the majority of cases)	Slightly below normal.

7. Stimulation of the adrenal cortex by ACTH

Although numerous pituitary hormones have been suggested by different workers as stimulators of the secretion of adrenocortical hormones, ACTH appears to be the only hormone with a direct action on the adrenal cortex, although an explanation of the mechanism is not yet forthcoming. From the clinical point of view this uncertainty is unimportant, since the activity of an ACTH preparation measured by SAYERS' ascorbic-acid method corresponds to its therapeutic activity^{8, 9, 11} and it is therefore largely irrelevant whether the preparation contains one or more active principles. It has, however, been established with certainty that a number of other pituitary hormones, now isolated in varying degrees of purity, have no direct action on the adrenocortical secretion. Among these are the gonadotropins, the growth hor-

mone, the posterior lobe hormones, etc. as well as the hormones of the adrenal medulla, the genital glands and the pancreas.

It is an established fact in endocrinology that the continuous administration of a hormone is itself a factor which increases the effect on the organ concerned. This arises from the fact that the endocrine-regulated organs require for normal functioning blood-hormone concentrations which are minimal, but constant in their action. Thus continuous intravenous infusion of ACTH has a much greater effect than subcutaneous injections at, say, 6-hourly intervals¹⁴⁻¹⁷. In practice, therefore, the administration of smaller doses at shorter intervals, or of larger doses in the form of a depot preparation, is to be recommended. When the patient exhibits immunity, or acquires immunity, with regard to a particular ACTH preparation, it should be replaced by one obtained from a different species of animal.

The adrenal cortex reacts to a single intravenous dose of ACTH with a rapid but short-lived increase in secretion. In man, for example, an increase of 300% in the total 11-17-O-corticosteroids in the renal veins has been observed in 30 minutes after an injection of 75 mg ACTH, after which the titre commences to fall³². Since the hormone must first be metabolized its effect reaches a maximum only after a delay of about 3 hours after the injection. The secretion returns to the normal level after 6 hours⁵⁸.

At the start of an ACTH therapy with single intramuscular doses spread over 24 hours, a step-wise increase in the urinary ketosteroids is usually observed, reaching a maximum after one or more days⁵⁹. It follows that the secretion of adrenocortical hormones must also increase gradually, but requires a number of separate impulses in order to reach full capacity.

The hormonal output of the adrenal cortex stimulated by ACTH consists of a spectrum of different hormones in which hydrocortisone and to a lesser extent corticosterone clearly predominate⁶⁰. From the clinical standpoint the action of ACTH can therefore be considered as broadly equivalent to that of hydrocortisone⁶¹ (cf. section 12, page 186). There is now evidence that the rate of secretion of aldosterone, however, remains independent of ACTH stimulation²⁵⁵.

8. Regulation of the activity of the pituitary-adrenal system

a) Autonomic humoral regulation. The ACTH-secretion of the pituitary is influenced, in inverse proportion, by the corticosteroid titre in the blood. Thus an increase in the corticosteroid titre, for example, results in a decrease in the ACTH-secretion^{10, 62-64}. The pituitary reacts thereby, not uniformly to the whole adrenocortical hormone spectrum, but principally to the 11-17-O-corticosteroids. The other known adrenocortical hormones, corticosterone, dehydrocorticosterone, cortexone and aldosterone⁶⁵, exercise an effect (decreasing in this order) insignificant in comparison with that of the 11-17-O-corticosteroids. It is not known whether the pituitary reacts directly to the corticosteroid titre or through the intermediary of a metabolite the titre of which is controlled by that of the corticosteroids⁶³. The pituitary does not react, for example, to the normal variations in blood of adrenaline, aminoacids, glucose or sodium⁶⁶.

The autonomic regulation between pituitary and adrenal cortex depends on changes of a quantitative nature⁶⁷, inasmuch as in stress (see section 11) reduction of the increased ACTH-secretion requires larger amounts of hormones. Whether in stress the stimulation threshold of the pituitary is actually higher, or whether this quantitative change is merely simulated by the increased need of the body for adrenocortical hormones, is not yet known.

The autonomic humoral regulation of the pituitary-adrenal system in stress is remarkably independent of any central or vegetative influence. It remains normal after severance of the infundibulum⁶⁸⁻⁷¹, after transplantation of the pituitary to the anterior chamber of the eye^{11, 69, 72, 73}, after total sympathectomy^{70, 74, 75}, after blocking of the sympathetic by antiadrenergics such as dibenamine (NN-dibenzyl-β-chloroethylamine, blocks adrenaline and noradrenaline but has a certain stimulating effect on the central nervous system) or tetraethylammonium chloride⁷⁶ (blocks the sympathetic ganglia) or ergotamine tartrate⁷⁷, while barbiturate anaesthesia suppresses solely the stress reactions due to cold⁷⁸ and spinal anaesthesia⁷⁹.

Adrenocortical hormones inhibit ACTH secretion probably by direct action on the pituitary, although the effect may be mediated by the hypothalamus. A reduced concentration of these hormones in the tissues has the effect of releasing the pituitary from inhibition, but this effect in itself cannot cause as great a stimulation of ACTH secretion as that which occurs in response to stress. It has been postulated that such rapidly acting stimuli of ACTH secretion may act through a chemotransmitter largely independent of the blood level of adrenocortical hormones²⁵⁴.

b) Central and vegetative regulation. Electrical stimulation of certain hypothalamic centres results in increased ACTH-secretion⁸⁰⁻⁸² and gonadotropin-secretion^{83, 84}. Direct electrical stimulation of the pituitary has no such effect⁸⁴. Stimulation of the sensory nerves likewise causes increased ACTH-secretion⁸⁵, as does psychic tension (drivers in motor racing⁸⁶) or fear or anger (rat¹⁰). On the

other hand, panhypopituitarism and a non-reacting pituitary have been observed in a case of pharyngioma of the hypothalamus⁸⁷ which was not affecting the pituitary. It follows that the hypothalamus must be capable of influencing the hormonal secretion of the pituitary.

No nervous connection exists between the hypothalamus and the anterior pituitary. Only the blood vessels of the *pars distalis* are sympathetically innervated⁸⁸, and these have no connection with the secreting cells. Although a direct nervous influence can thus be excluded, a direct neurohumoral connection is possible since the blood-stream^{89, 90} in the portal vascular system of the pituitary flows in the direction hypothalamus → pituitary. The loss of anterior pituitary function which is observed when the portal blood-flow is interrupted could be an argument in support of this hypothesis⁹¹, if indeed this loss of function is not due, as is more likely, to ischaemia of the pituitary consequent upon interruption of the blood-flow^{92, 93}. *It is not yet possible therefore to decide whether there exists a direct neurohumoral connection between hypothalamus and pituitary.*

An indirect influence via the neurovegetative system, or a direct influence of this system itself, may be possible in view of the known effect of adrenaline on ACTH-secretion. Whether directly applied to the pituitary^{11, 94} or injected intravenously^{70, 85, 95-100} et al., adrenaline causes an increase in the ACTH- and LH-^{101, 102} secretions.

The action of adrenaline on the LH-secretion can be blocked by antiadrenergics (dibenamine), as can the electrically-induced hypothalamic impulse¹⁰². Adrenaline and noradrenaline appear for this reason to be involved in some way in the regulation of the gonadotropin-secretion by the hypothalamus and/or the neurovegetative system.

On the other hand this does not appear to be the case in the regulation of the ACTH-secretion: 1. The regulation is not blocked by substances with antiadrenergic or similar activity (see under a); 2. Total sympathectomy does not affect the regulation (see under a), nor does it affect the increase of secretion evoked by electrical stimulation of the hypothalamus⁸²; 3. It would be hardly understandable that histamine^{103, 104}, pitressine or ether¹⁰³, for example, cause an increase of ACTH-secretion more rapidly than adrenaline⁹⁹; in these circumstances transmission of an alarm impulse by the neurovegetative system is out of the question. *For these reasons it is unlikely that adrenaline plays any part in the neurohumoral transmission of the impulses, either central or vegetative, which regulate the ACTH-secretion of the pituitary.* The significance of adrenaline could, however, lie in its sustaining and reinforcing effect¹⁰ on the autonomic regulation described under a) above, following a stress which alarms the neurovegetative system. This effect would be in accordance with the following scheme: the hypoglycaemia resulting from stress alarms the neurovegetative centres, the secreted adrenaline mobilizes the liver glycogen and thereby increases the need for glyconeogenesis; this in turn calls for an increase in the output of adrenocortical hormones in order to render further glyconeogenesis possible from the reserve of proteins in the body. Support is lent to this hypothesis by the observation¹⁰⁵ that insulin treatment of starving rats releases an adrenaline secretion from the medulla amounting to 30 µg in 4 hours.

Summarizing, the following conclusions can be drawn: The pituitary-adrenal system regulates its activity by means of an autonomic humoral mechanism not yet elucidated, and is in this respect remarkably independent of central or vegetative influence or support.

The deeper significance of the function of the pituitary-adrenal system, a function independent of central regulation, becomes clear when the role of the adrenocortical hormones is seen to be that of maintaining homeostasis (see section 11).

Central and vegetative influences over the pituitary-adrenocortical activity have been demonstrated, but their mechanism is not yet understood.

It cannot be ruled out that adrenaline, and perhaps other substances, when administered in strong overdoses may affect the ACTH-secretion of the pituitary. In physiological doses adrenaline merely reinforces, indirectly, the autonomic regulation of the pituitary-adrenal system.

The hormonal activity of the pituitary-adrenal system is disturbed by exogenous administration of hormones as a result of its autonomic regulation. Exogenous ACTH in large doses has a depressing or inhibiting effect, by way of the adrenal cortex, on the endogenous*

* Exogenous administration of hormones with the endocrine glands intact must on principle be considered as equivalent to an overdose of hormones.

ACTH-secretion. Exogenous corticosteroids in large doses have likewise a depressing or inhibiting effect (cf. the varying sensitivity of the pituitary to different corticosteroids mentioned at the beginning of this section) by way of the pituitary and adrenal cortex, on both the endogenous ACTH-secretion and the hormonal secretion of the adrenal cortex.

In cases of adrenogenital syndrome the possibility therefore exists of moderating the abnormal spectrum of endogenous adrenocortical hormones by means of exogenous 11-17-O-corticosteroids, provided that the adrenal dysfunction does not have its origin in a neoplasm^{106,242-244}.

9. Morphological changes in the pituitary and adrenal cortex resulting from their activity

Glandular activity is accompanied by morphological changes in the glands. Autopsies have revealed an adrenal cortex hypertrophied¹⁰⁷ after ACTH therapy and stress and atrophied^{107,109} after cortisone therapy. The corresponding morphological changes affected mainly the fasciculate and reticulate zones, while the glomerular zone was only slightly affected if at all. These changes are reversible¹⁰⁹.

Basophil adenomas with hyaline degeneration, similar to those in a spontaneous CUSHING's syndrome^{110,111}, have been observed in the pituitary after ACTH therapy.

These morphological changes may be the origin of the ADDISON-like symptoms^{42,112} which are observed after cessation of a prolonged ACTH or 11-17-O-corticosteroid therapy. The following clinical precautions should therefore be taken: 1. At the conclusion of an ACTH therapy the doses should be gradually reduced in order to allow a gradual recovery of the pituitary; 2. At the conclusion of an 11-17-O-corticosteroid therapy, concurrently with the gradual reduction of the exogenous corticosteroids, the adrenocortical activity should be rapidly restored to normal level by means of ACTH, and the treatment ended with a gradual reduction of the ACTH doses.

10. Pituitary relations between the pituitary-adrenal system and other hormonal systems

Only three types of cell occur in the anterior lobe of the pituitary. Certain cells must therefore produce several different trophic hormones, and it is very probable that the output of one hormone can only be increased at the expense of the others, particularly when the increase exceeds certain limits. Observations which support this supposition are, for example, the diminished stress reaction in castrated mice¹¹³ (diminished ACTH-output due to excessive gonadotropin production?); atrophy of the gonads following X-ray treatment (increase of ACTH-output after X-ray stress at the expense of gonadotropins?)¹¹⁴.

In apparent conflict are the following observations: cold stimulates the secretion both of ACTH and thyrotropic hormone⁷⁷; exogenous thyroprotein in physiological doses at 24°C results in a significant enlargement of the adrenal cortex, at 30°C in a significant shrinking²⁵³; the thyroid function is lowered by ACTH and hypothyroses are frequently observed^{100,115-119} (masked by the increase in basal metabolism due to ACTH¹¹⁹) which can usually be eliminated by administration of thyrotropic hormone¹²⁰ (inhibition of the total pituitary hormone secretion when the secretion of a trophic hormone is arrested by an exogenous administration?); and the known facts that ACTH therapy usually inhibits protein output (as previously, inhibition of the growth hormone output?) and occasionally causes loss of libido and cessation of menstruation.

The correlation of the various hormonal systems in the pituitary still requires experimental elucidation. In the light of present knowledge, however, the following clinical precautions are indicated: in prolonged ACTH or hydrocortisone/cortisone therapy attention should be paid to the possible emergence of disturbances of the hormonal equilibrium of pituitary origin, particularly masked hypothyroses. In short-term therapy disturbances of the hormonal equilibrium are more probably of cellular origin, caused as a rule by defective functioning of a gland producing an antagonistic hormone, such as the pancreatic islets.

11. Significance of the pituitary-adrenal system

With the adrenal cortex intact the organism is capable of responding to a great variety of demands ("stressess"*) regardless of their nature, so long as a majority of the body cells are affected sympathetically ("systemic" stress*) either directly and uniformly ("non-specific" stress*) or via specifically sensitive groups of cells such as a vital organ ("specific" stress*). The defensive reactions show remarkable similarity from one case to another, even when there is a deficiency of nervous centres. These stress reactions^{45,63,121-124} consist of, *inter alia*, negative nitrogen balance; disturbed (inhibited) carbohydrate uptake; ketosis and (in prolonged severe stress) fatty degeneration of the liver; water retention; negative potassium balance with hypochloraemic hypokalaemic alkalosis; involution and arrested growth of the lymphatic tissues and organs; eosinopenia; increased urinal elimination of corticosteroids. These symptoms are identical with those observed after exogenous administration of ACTH/adrenocortical hormones, i.e. after overdoses of these hormones**¹²⁵. Under stress the ACTH-secretion is increased (cf. section 8) so that considerable quantities of adrenocortical hormones become available to the body; the adrenalectomized or adrenal-deficient organism on the other hand shows a severe and immediately apparent slowing-down of all the metabolic processes, so that it is deranged by the slightest influences. For these reasons the widespread deduction that the stress reactions are specific effects of the adrenocortical hormones would appear to be logical. This deduction is incorrect, however, as the following observations show.

The purpose of the stress reactions can only be to increase the defensive capacity and resistance of the body in an emergency. If they were in fact effects of the adrenocortical hormones, then administration of moderate doses of these hormones should strengthen the defensive reaction and resistance. This is, however, not the case¹²⁶⁻¹²⁷ unless the organism is in a state of fatigue due to previous demands. The adrenalectomized animal kept alive by means of constant doses of adrenocortical hormones reacts normally to stress^{122,128-131}. In this case the quantity of hormones available to the organism is constant and cannot possibly control the dynamics of the stress reactions. ACTH/adrenocortical hormones thus render possible the stress reactions but do not actually bring them about¹³². In other words, *adrenocortical hormone is not the specific cause of the stress reactions and is not therefore responsible for the effects resulting from overdoses of ACTH/adrenocortical hormones.*

After severe overdoses of adrenocortical hormones the body reacts to minor demands of a kind to which it would not react without the exogenous hormone, while in cases of severe stress even excessive overdoses of hormones cannot further intensify the stress reaction¹²⁸. In adrenalectomized animals kept alive by means of salt solutions, involution of the lymphatic tissues is not observed as a stress reaction; after subliminal doses of adrenocortical hormones this reaction follows promptly¹³³. These observations also demonstrate clearly the non-specificity of the adrenocortical hormones; at the same time they show that *these hormones sensitize the organism to stress*. The literature contains numerous other ex-

* Systemic stress can be non-specific, specific, or both. For many demands the latter will be the case, with the emphasis either on the non-specific component (e.g. in X-ray treatment) or on the specific component (e.g. in neurointoxication or extirpation of the thyroid). In the literature the expressions specific and non-specific are commonly used in connection with stress, but systemic stress is implicitly understood.

The following are included under stress: severe psychic excitation, severe muscular exertion, traumatic shock (accidental, obstetric, surgical, medicamentous, etc.; mechanical, haemorrhagic, electrical, toxic; burns, frostbite; shock due to acceleration, large pressure changes, etc.), exposure to heat and cold, exposure to ionizing radiations, diathermy, ultra-sound, anoxia, haemorrhage, infections, allergic effects, overdoses of hormones, malnutrition, hunger, thirst, severe atmospheric effects, severe exposure to the sun, etc. In this connection see SELYE, H., *Stress*, Montreal, 1950.

** Exogenous administration of hormones with the endocrine glands intact must on principle be considered as equivalent to an overdose of hormones.

amples of the non-specificity of the adrenocortical hormones. Thus the same dose of adrenocortical hormone can promote protein formation in adrenalectomized animals (anabolic effect), or have no effect on protein metabolism when the diet is rich in carbohydrates; the same dose can have a small but significant effect on starving rats, or cause a large increase in protein metabolism when the rats are subjected to a stress^{134,135}; the negative N-balance can be eliminated by increasing the intake of carbohydrate¹³⁵, amino-acids¹³⁵ or potassium¹³⁶, or by administration of testosterone⁴²; the elimination of ketosteroids in the urine is increased or diminished by corresponding changes in the intake of salt⁶⁰; eosinophil depression may be absent in ACTH therapy, but may appear suddenly if a renal colic develops during the treatment¹²⁸ (discussion); an eosinophil depression has also been observed in adrenalectomized animals¹³⁷ and in ADDISON's disease⁷⁰ after injection of adrenaline, as well as in hypophysectomized mice¹³⁸.

The physiological effects of ACTH/adrenocortical hormones, with a few exceptions, also appear to be non-specific. This is illustrated by the foregoing examples in respect of lymphatic tissue and eosinophil depression, and by the following observations: adrenocortical hormones retain their action on eviscerated animals¹²², and on the isolated spleen¹³⁹ and liver¹⁴⁰; the psychic disturbances occasionally observed under ACTH/adrenocortical hormone treatment can be prevented or eliminated by increasing the potassium intake⁶⁰. The physiological effects of overdoses of ACTH/adrenocortical hormones* extend over the whole organism and are particularly marked in the organs derived from the primitive mesenchyme (connective tissue, synovial membranes, reticulum, blood-vessels, lymphatic tissues and organs, muscle), presumably because the mesenchyme is particularly susceptible to the metabolic effects made possible by adrenocortical hormones.

The physiological effects of overdoses of adrenocortical hormones* are, *inter alia*, involution or retarded development of the lymphatic tissues and organs^{141,142}, transitory leucopenia¹⁴³, eosinopenia⁹⁷, retardation or arrest of granular and somatic development and of the tendency to inflammation and allergy, acne, diminution or inhibition of fever, analgesia, slightly increased blood-pressure, bradycardia, but tachycardia during muscular exertion, increase of irritability up to psychic disturbances with or without EEG-changes, increased pepsin elimination, lowered cell permeability.

The fact that adrenocortical hormones affect the whole organism, and the non-specificity of their metabolic effects, appear to indicate attack at the level of the cell (cell permeability?), although this is at present a purely speculative assumption. On the other hand the tendency in all reactions set in train by ACTH/adrenocortical hormones is clearly *an immediate increase of the power of resistance in an emergency* (above all by increasing not only the potential energy immediately disposable, and thereby the peripheral circulation, but also the psychic reactivity) *at the expense of vital functions which are less important or even a hindrance in an emergency* (healing of wounds, sensitivity to pain, resistance to inflammation, etc.).

The foregoing has shown that the pituitary-adrenal system occupies a prominent position in the hierarchy of regulators¹⁴⁴ which are doubtless collectively responsible for the maintenance of homeostasis^{145,146}. That the pituitary-adrenal system and the other still unknown co-regulators are very largely independent of the nervous centres, is shown by the fact that the stress reactions, with very few exceptions, are normal when none of the nervous centres is operative. Summarizing:

The adrenocortical hormone is a hormone responsible, in the broadest sense, for the maintenance of homeostasis. It acts as a sensitizer which enables the organism to react to internal and external demands, and as a promoter of the appropriate defensive reactions, without actually being specific for these reactions.

The role of the pituitary-adrenal system is that of adjusting the output of the adrenocortical hormone to the needs of the organism and assuring its sufficiency in an emergency. This is achieved by an extremely sensitive autonomic regulation which is largely independent of the nervous centres.

This hypothesis provides an explanation and an evaluation of the multiple, often seemingly complex effects of the adrenocortical hormones, and of the function of the pituitary-adrenal system, in harmony with experimental and clinical observations.

12. Pharmacological effects of exogenous administration of ACTH/adrenocortical hormones* with intact pituitary-adrenal system

Since ACTH/adrenocortical hormones sensitize the organism to stress, and since minor stimuli are always present, exogenous administration of these hormones* brings about a stress reaction proportional to the dose administered. This reaction is not consistent with the internal and external demands on the organism and is thus useless. *No increase in bodily resistance is thereby achieved, since the intact pituitary-adrenal system in any case adjusts the hormonal secretion automatically to the internal and external demands, thus conferring optimal defensive resistance on the body. With the pituitary-adrenal system intact no increase in bodily resistance can therefore be expected from the exogenous administration of ACTH/adrenocortical hormones*; the only therapeutically useful effects are those individual stress reactions, or a group of these reactions, in symptomatic therapy, or the warning effect of the stress reaction in alternative therapy.* On the other hand a causal therapy is indicated in case of accidental failure of a normal pituitary-adrenal system (acute and relative insufficiency), as a consequence of abnormal demands or in ADDISON's disease (cf. section 13).

When, as in symptomatic therapy, exogenous administration of ACTH/adrenocortical hormones is resorted to as a result of individual stress reactions, or groups of them, other stress reactions not utilizable in the particular case will appear and will exercise a disturbing effect in proportion to the doses which have to be administered. Since these secondary effects form a biological entity with those that it is desired to produce, they will not be differentiated in the discussion which follows.

Differences in the effects of various adrenocortical hormones and of ACTH

Aldosterone⁶⁵ and cortexone have the strongest and cortisone the weakest electrolyte effect**; ACTH and hydrocortisone have an approximately equal electrolyte effect⁶¹, more marked than that of cortisone but much weaker than that of cortexone. Corticosterone¹⁴⁷ stands midway between cortisone and cortexone, with a weaker electrolyte effect than ACTH or hydrocortisone.

ACTH, hydrocortisone and cortisone have almost equal effects on organic metabolism, cortexone has the least effect, and corticosterone stands midway between the two extremes.

Cortexone is a precursor of corticosterone⁶⁰, and can thus be regarded as a by-product of the synthesis of corticosterone in the adrenal cortex, only appearing in small quantities in the blood. Cortisone, on the other hand, is a degradation product of hydrocortisone⁶⁰; it can be assumed to be present in the organism effectively in larger amounts, although it is only secreted in small quantities. Exogenous cortisone can apparently be converted in the organism into hydrocortisone (liver)^{148,149,150}. Corticosterone and hydrocortisone are the end-products of a double synthetic process in the adrenal cortex in which the synthesis of hydrocortisone, when strongly promoted by ACTH, inhibits that of corticosterone⁶⁰.

Cortexone and corticosterone may only be prescribed in ADDISON's disease, and none of the following observations apply to them. Hydrocortisone and cortisone are understood under the name adrenocortical hormones. Unless otherwise stated, the effects of these two hormones and of ACTH may be considered as practically the same.

Hydrocortisone, cortisone, and corticosterone (as pure hormones, i.e. alcohols – not acetates) are fully effective both orally and parenterally^{147,151–153}, cortexone only parenterally or lingually³⁶. Orally, hydrocortisone (alcohol) is weight for weight about twice as effective as cortisone.

* Exogenous administration of hormones with the endocrine glands intact must on principle be considered as equivalent to an overdose of hormones.

** The Na-retention of aldosterone is ca. 25 times greater, the K-retention ca. 5 times greater, than that of cortexone. Aldosterone, in contrast to cortexone, has no effect on water elimination⁶⁵. Cortexone has an electrolyte effect ca. 50 times greater than that of cortisone⁵².

Electrolyte and water metabolism^{122,123}

Physiologically the adrenocortical hormones have a diuretic and salt-retaining function and are in this respect antagonistic to (but not correlated with) the antidiuretic and salt-eliminating hormones of the posterior pituitary¹³⁷. This function is shown clearly in patients with ADDISON's disease, who owing to adrenocortical insufficiency can no longer respond to water-loading with the usual increase in diuresis³⁶. Adrenocortical hormones immediately restore the normal diuretic response^{36,154}. Exogenous ACTH or adrenocortical hormones, i.e. overdoses of adrenocortical hormones, disturb the hormonal equilibrium mentioned earlier. Salt-retention becomes excessive, with consequent compensatory water-retention thus masking the diuretic effect of these hormones. This provides an explanation of why the unwelcome secondary effects (described below) with regard to electrolyte and water metabolism in ACTH/adrenocortical hormone therapy can be avoided by means of a diet low in salt.

At the commencement of therapy ACTH and hydrocortisone lead to a marked *retention of salt and water*⁴⁶, diminishing during long treatment, but usually persistent. Cortisone has the same effect but to a lesser degree, and in this case prolonged treatment may result in the retention being replaced temporarily by an increased elimination¹⁵⁵. Symptoms: increase in body weight, oedema, haemodilution (lowering of haematocrit value, electrolyte values usually only slightly changed; change in serum electrolyte values usually only in prolonged treatment or with large doses), lowered diuresis. These symptoms can be largely prevented or eliminated by a diet low in salt.

Combined with the foregoing are *negative potassium balance* and increased phosphate elimination. This effect too is more marked at the commencement of therapy, persists to a lesser degree throughout the treatment, and can lead to a considerable potassium impoverishment. Symptoms: the potassium impoverishment is indicated, before it can be detected chemically, by a heightened nervousity* and psychic irritability, possibly leading to psychoses with or without EEG-changes⁶⁰. With large doses a hypochloroemic hypokalaemic alkalosis due to the electrolyte changes is observed on rare occasions.

In *newborn infants*, in contrast to adults and children, the K- and Na-elimination under ACTH/adrenocortical hormone treatment is *not* increased, but diminished. All other hormonal effects, such as increased elimination of 17-ketosteroids, effect on reactive processes, etc. are the same as in adults¹⁵⁶.

In the tissues the following electrolytic changes have been observed¹⁵⁷: *muscle*: extracellular sodium, chlorine and water content increased, intracellular potassium and phosphorus content decreased, intracellular sodium unchanged; *erythrocytes*: sodium increased, chlorine unchanged, potassium decreased. Symptoms: muscular weakness, including myocardium; electrocardiographic changes; bradycardia, but tachycardia during muscular exertion^{157,158}. The changes in potassium metabolism mainly follow those in N-metabolism. Administration of potassium not only prevents, or eliminates, the above symptoms but also normalizes the negative N-balance, while conversely normalization of the N-balance improves but cannot quite normalize the negative K-balance¹⁵⁹.

From the clinical point of view the following are accordingly recommended: control of urine from the commencement of treatment until equilibrium is restored, *diet low in salt, potassium administration*; attention should be paid to the risk of apoplexy and cardiac or circulatory insufficiency, although these conditions do not constitute an absolute contraindication. *Oedema must not be treated with diuretics, since the potassium deficiency will be greatly increased thereby.*

Nitrogen metabolism^{122,123}

ACTH/adrenocortical hormones have an antianabolic effect, i.e. they inhibit protein formation and lead to *intensified protein*

metabolism with negative N-balance. The residual blood nitrogen, particularly the amino-acid fraction, is increased^{155,160}.

The negative N-balance is less marked in man and its magnitude is dependent on the doses administered¹⁵⁹. It may be prevented or eliminated by administration of potassium¹³⁶ or testosterone⁴², or by increasing the intake of calories¹⁶¹ or amino-acids¹³⁵. The amino-acid fraction of the residual nitrogen remains high, even when the N-balance is normalized¹⁶⁰.

Under ACTH/adrenocortical hormone treatment a sharp rise in uric acid elimination is observed, due mainly to increased renal clearance^{162,163} and to a lesser extent to the increased N-metabolism. Amino-acid elimination is likewise increased¹⁵⁵.

The retardation of granular and somatic growth observed with large doses of ACTH/adrenocortical hormones is very probably due to the catabolic action of these hormones^{123,164}.

Abnormal plasma-protein spectra in rheumatoid arthritis and other diseases can be corrected by ACTH/adrenocortical hormone therapy¹⁶⁵⁻¹⁶⁷. A marked and sudden fall in β -globulins is often observed^{166,168}.

In cases where ACTH/adrenocortical hormone therapy is indicated on account of its growth-retarding effect and where large doses must therefore be administered, it is advisable from the clinical point of view to normalize the negative N-balance either by modifying the diet (see above) or by means of testosterone, or both.

Carbohydrate metabolism^{122,159,169}

In ACTH/adrenocortical hormone treatment there is an *increase in blood sugar and in glycogen storage in the liver* (increased liver glycogen only in treatments of short duration, since the storage is transitory¹⁴¹), but muscle glycogen remains unchanged. It follows that in some cases a diabetes may develop¹⁷⁰ or a pre-existent diabetes may be aggravated¹⁷¹. Normally the capacity of the pancreatic islets is large enough to paralyse the diabetogenic action of the ACTH/adrenocortical hormones, so that the blood sugar is only slightly increased, if at all. There is no danger of persistence of such an induced diabetes after cessation of the therapy¹⁵⁹. The majority of patients in whom a diabetes is induced in this way belong to diabetic families (anamnesis). ACTH/adrenocortical hormones are for this reason already being used for diagnostic purposes (latent diabetes).

The increased glycosuria inevitable in ACTH/adrenocortical hormone treatment is the result of an increased clearance^{170,172,173}, since the blood sugar is only slightly increased, if at all (see above).

From the clinical point of view it is therefore advisable to keep the sugar content of the urine and blood under control during the therapy; there is no contraindication for diabetics¹⁵⁹. The diabetogenic action of ACTH/adrenocortical hormones can be applied therapeutically in cases of spontaneous hypoglycaemia (mostly hereditary) if unaccompanied by ADDISON's disease¹⁷⁴, as also in other hypoglycaemic conditions such as myotonic dystrophy¹⁷⁵.

Fat metabolism

ACTH/adrenocortical hormones have an effect on fat metabolism, but little is known of this effect. The hormone appears to condition the mobilization of fat, but is not the causative agent¹⁷⁶. It brings about a regular reduction in the subcutaneous fatty tissue^{122,177} and increases liver fat under a diet rich in carbohydrates^{142,178} (but not under a protein-rich diet¹⁴²). It also increases fat in the interscapular gland (rats)¹⁷⁹ and in bone marrow¹⁸⁰ (the latter probably as a result of the regressive changes in bone marrow following overdoses of ACTH/adrenocortical hormones).

* The euphoria often observed in ACTH/adrenocortical hormone therapy is mainly due to the symptomatic improvement in the general condition.

The ketone content of the blood is increased. In man this results only in a transitory ketosis^{52,181}. The capacity of the organism to utilize ketones is apparently even increased by hormone therapy¹⁸¹.

Histological and morphological effects on the organs

ACTH/adrenocortical hormones affect particularly the organs derived from the primitive mesenchyme: lymphatic tissue, bone marrow, connective tissue, synovial membranes.

a) *Lymphatic tissue*. The hormone provokes a *marked involution of the lymphatic organs*, whereby the parenchymatous cells as well as those of the reticular connective tissue are affected¹⁴². Two phases can be distinguished: at the commencement of therapy there occurs a characteristic degeneration of the thymocytes of the thymus and of the lymphocytes of the lymphatic ganglia, an effect less marked in the spleen¹⁸². The second phase, following this lymphocytolysis, is characterized on the one hand by inhibition of the growth of new cells, manifested by absence of mitoses in the thymus, lymphatic ganglia and spleen, and on the other hand by degeneration of the reticular connective tissue. Lymphocytolysis and the consequent growth inhibition are responsible respectively for the increase in serum antibodies at the commencement of therapy and for the subsequent decrease in the same after prolonged therapy.

b) *Bone marrow*. In experimental animals (rats) ACTH/adrenocortical hormones cause extreme involution of the red bone marrow¹⁴¹.

c) *Supporting connective tissue* (cartilage, bone). Adult cartilage is little affected. The proliferation, resorption and invasion of the connective tissue of bone marrow in the developing epiphyses of the long bones are inhibited¹⁴¹. Osteoporosis has been observed¹⁸³.

d) *Elastic connective tissue* (skin). ACTH/adrenocortical hormones bring about a more compact disposition of the collagenous fibres and a modification of their form¹⁷⁷. The growth of the epithelial organs of the skin is inhibited, the epidermis becomes thinner, the growth of hair ceases; the sebaceous glands are less affected (rats)¹⁴¹.

Adrenocortical hormone in alcoholic solution *locally applied* affects all components of the connective tissue for a period of up to 160 days: the number of fibroblasts is reduced, the skin as a whole becomes thinner, the collagenous fibres fuse to a compact mass (rats)¹⁸⁴.

e) *Gastro-intestinal tract. Stomach*. The mucosa becomes markedly thinner, particularly the epithelial layer¹⁴¹. Since the latter secretes the protective mucus the frequent occurrence of gastric ulcers during ACTH/adrenocortical hormone treatment probably arises from insufficient protection of the mucosa against HCl. Moreover, the basal secretion of HCl and pepsin in an ACTH treatment (e.g. with doses of 100–160 mg/day during 3–4 weeks) rises to the level of that in patients with gastric ulcers (with simultaneous increase of uropepsin elimination¹⁸⁵).

Duodenum. The intestinal villi become distended, the epithelial cells vacuolized. The epithelial layer becomes separated from the connective tissue by a liquid containing proteins¹⁴¹.

Many of these and other changes^{186–188} following overdoses of ACTH/adrenocortical hormones resemble those occurring in starvation¹⁴¹. This may be due to the fact that the regressive changes in the gastro-intestinal tract affect sympathetically the resorption of nutriment, and that protein and fat catabolism are affected both in starvation and by overdoses of ACTH/adrenocortical hormones.

Effect on reactive processes

ACTH, hydrocortisone and cortisone have a *retarding or inhibiting effect on most inflammatory processes of toxic, allergic, infectious or other origin, combined with a marked analgesic action*. The mechanism of this

effect is not known, but it is purely symptomatic since the fundamental processes remain unaffected. Thus large doses of ACTH/adrenocortical hormones during ultraviolet irradiation, for example, inhibit only the erythema, not the eventual pigmentation¹⁸⁹.

The antigen-antibody reaction is likewise unaffected^{190–192}, as also the systematic anaphylactic reaction¹⁹³. The diminution in antibodies observed in prolonged treatment^{184,195} appears to arise from inhibition of synthesis rather than from increased degradation¹⁹⁶ (cf. lymphatic tissue, above).

ACTH/adrenocortical hormones have *no antihistaminic action*. They have no effect on urticaria or on skin tests which react to antihistaminics^{197–199}. On other skin tests the effect is variable. Thus reduction and/or suppression of the tuberculin test have been reported by some workers^{200,201} while others have reported no effect¹⁹³. The SCHICK test is not affected²⁰²; the passive ARTHUS phenomenon has been variously reported as inhibited¹⁹⁵ and unaffected¹⁹³. The inflammation-inhibitory and analgesic effects of ACTH/adrenocortical hormones give rise to the following, mainly symptomatic, therapeutic indications*:

a) in chronically inflamed conditions: rheumatoid arthritis^{151,152,167,203–208} etc. in which para-aminobenzoic acid has a synergic effect²⁰⁹; iridocyclitis and uveitis^{210–212}; periarteritis nodosa²¹³; shoulder-hand syndrome and periarthritis of the shoulder²⁰⁶; lupus erythematosus^{214–217}; generalized neurodermatitis²¹⁶;

b) for the checking of excessively acute inflammatory conditions capable of causing permanent lesions: rheumatic fever (acute rheumatism, rheumatic carditis – about the same effect as salicylate therapy^{203,218–220}); typhoid fever^{221,222};

c) for the checking of excessively acute inflammations which the body momentarily cannot overcome: extensive burns^{223–227} (see also²²⁸); snake-bite²²⁹;

d) for the checking of traumatic inflammations (chemical or due to foreign bodies) as preoperative treatment, e.g. in traumatic uveitis²³⁰;

e) for the symptomatic treatment of other acute inflammations: acute dermatomyositis²³¹; trichinosis²³²; herpes zoster²³³; tuberculous meningitis (+ adequate treatment with streptomycin and PAS)²³⁴; *contraindicated in other forms of tuberculosis***;

f) for the inhibition of allergic diseases and immunological reactions: asthma (for a review see²³⁵); no appreciable effect in other allergic diseases, nor in the inhibition of immunological reactions, e.g. no effect in skin grafting²³⁶.

ACTH/adrenocortical hormones have an *arresting or inhibiting effect on growth*, an effect which appears only when large doses are administered. This effect can be applied therapeutically for the inhibition of undesirable granulations, growths, etc. With normal doses there is no danger of any retardation in the rate of healing. *Closely linked with this effect is the depressive effect on all lymphatic tissues and organs*. These hormones are consequently indicated in acute leukaemia^{237,238} and other malignant diseases of the lymphatic tissues. Only temporary remissions, however, are to be expected.

ACTH/adrenocortical hormones possess likewise a marked effect, not yet fully elucidated, on haematopoiesis. At the commencement of therapy a reticulocyte crisis usually appears, presumably as a result of direct action on the spleen²³⁹ (simultaneous thrombocyte crisis and eosinopenia). These hormones thus have a favourable effect on thrombopenic purpura²⁴⁰.

The general stress reaction due to ACTH/adrenocortical hormones can also be applied in alternative therapy, for example in refractory anaemia²⁴¹ and insulin-resistant diabetes²⁴⁵. *The danger exists, however, that latent infections may thereby be reactivated or propagated (e.g. tuberculosis or malaria)*. In ACTH/adrenocortical hormone therapy it should always be borne in mind that intercurrent diseases may be masked by the anti-inflammatory and analgesic effects of these hormones²⁴⁶. A further undesirable secondary effect arises in the intestinal organs, as evidenced by a number of observations, in that

* Only those indications are given in which the use of ACTH/adrenocortical hormones has been shown to add considerably to the therapeutic possibilities.

** Except in cases of ADDISON's disease.

gastric or intestinal ulcers may spontaneously perforate, or that spontaneous perforations may occur without ulcers in the anamnesis, or that postoperative sutures may become slack (cf. histological and morphological effects, previous page). This effect is all the more dangerous in that peritonitis, masked by the effect of the hormones, may develop either without symptoms or merely with slight pain of no apparent significance (no abdominal tension). *Clinically, it is therefore advisable in ACTH/adrenocortical hormone therapy to investigate carefully the slightest abdominal pain; it follows, further, that these hormones are absolutely contraindicated for patients who are suffering, or have suffered, from gastrointestinal ulcers*.*—Frequent thromboses have also been observed after the cessation of postoperative ACTH/adrenocortical hormone therapy, whereas they are extremely rare during the therapy²⁴⁷. (Possibly an increased tendency to thromboses is a natural result of the return to normal adrenocortical secretion in postoperative convalescence.)

13. ACTH/adrenocortical hormones in insufficiency of the pituitary-adrenal system

Marked secondary (pituitary-conditioned) or primary adrenocortical insufficiency is very rare. Opinions differ as far as relative insufficiency is concerned, but it is likewise generally considered to be rare. It has been observed after severe operations (unsatisfactory convalescence) and in cachectic patients after several months of illness^{247, 248}. It cannot be diagnosed with certainty by current tests since these give a measure only of functional ability, not of functional capacity or reserve. *It is, however, certain that there has been no question of a relative insufficiency in any of the diseases which up to now have been successfully treated with ACTH/adrenocortical hormones* (with the exception, of course, of those in which there is a marked insufficiency, such as ADDISON's disease)¹⁵⁹.

In cases of sudden severe stress, such as major operations, accidents, etc., which almost exceed the normal defensive capacity of the organism, exogenous ACTH/adrenocortical hormone is indicated, *but not as a substitute for any of the measures usually adopted in such circumstances*²⁴⁷.

ACTH/adrenocortical hormone therapy has been successfully applied as *substitution therapy in SIMMONDS' disease*²⁴⁹.

Corticosterone (orally, often sufficient without other complementary adrenocortical hormone)²⁵⁰ and cortexone + cortisone^{36, 53, 251} (dosage flexible, depending on bodily demands) can be employed as *substitution therapy in ADDISON's disease*.

THORN's eosinophil test²⁵² is a suitable test for the functional capacity of the adrenal cortex: the eosinophils are counted immediately before and 4 hours after an injection of 25 mg ACTH; a 50% fall is the lower limit of the normal. Only a positive result may be considered as a specific indication of adrenocortical function. A negative result may be due to a refractory eosinophilia.

The latter possibility can be excluded by making a similar test with 50 mg cortisone taken orally. A fall of more than 50% then clearly indicates adrenocortical insufficiency.

In the event that this test also yields a negative result either the THORN test should be repeated in conjunction with observation of the urinary ketosteroids and corticosteroids, or the 48-hour THORN test should be applied, with the initial dose of 25 mg ACTH followed at 6-hourly intervals by further injections of 10 mg. Observations are made of the percentage eosinophil depression during the 48-hour period, as well as of the increase in urinary ketosteroids. Adrenocortical insufficiency is indicated by a 90% drop in eosinophils accompanied by a considerable increase in urinary ketosteroids. In ADDISON's disease the eosinophil depression does not reach the 50% limit and the ketosteroid elimination is less than 3 mg/24 hours. (Cf. Na/K-ratio in saliva, page 283.)

Adrenaline is often used to bring about eosinophil depression in place of ACTH. This substance acts *indirectly* and its mode of action is not known with certainty. It should therefore *no longer be used* for this purpose since it may yield deceptive results; eosinophil depression has been caused by adrenaline, for example, in patients with total adrenalectomy¹³⁷ and ADDISON's disease⁷⁰ (very probably by action on the spleen). See also sections 8(b) and 11.

* The danger occurs apparently only in the upper intestine; good symptomatic results have been observed, for example, in ulcerative colitis. A bibliography on ACTH is to be found on the following pages.

Bibliography

- 1) LI et al., *Nature*, **173**, 251, 1954.
- 2) LI et al., *Nature*, **176**, 687, 1955.
- 3) BELL, P. H., *J. Amer. chem. Soc.*, **76**, 5565, 1954.
- 4) WHITE, W. F., and LANDMANN, W. A., *J. Amer. chem. Soc.*, **77**, 1711, 1955.
- 5) BRINK et al., *J. Amer. chem. Soc.*, **75**, 1960, 1953.
- 6) MUNSON et al., *Fed. Proc.*, **9**, 208, 1950.
- 7) SAYERS et al., *J. biol. Chem.*, **149**, 425, 1943.
- 8) OSTERLING and LONG, *Science*, **113**, 241, 1951.
- 9) PRUNTY et al., *J. Endocr.*, **7**, xxii, 1951.
- 10) LONG, C. N. H., *Recent Progr. Hormone Res.*, **7**, 75, 1952.
- 11) McDERMOTT et al., *Yale J. Biol. Med.*, **23**, 52, 1950.
- 12) LONG, C. N. H., *Recent Progr. Hormone Res.*, **1**, 99, 1946.
- 13) SPIERS et al., *Clinical ACTH*, vol. **1**, 32, 1951.
- 14) HOLLANDER et al., *Endocrinology*, **49**, 617, 1951.
- 15) HENLY and POTTER, *Lancet*, **1**, 697, 1952.
- 16) BURTON et al., *J. biol. Chem.*, **193**, 769, 1951.
- 17) BUSH, I. E., *Biochem. J.*, **50**, 370, 1952.
- 18) HÜBENER et al., *Hoppe-Seyl. Z. physiol. Chem.*, **289**, 102, 1952.
- 19) NELSON et al., *Science*, **111**, 578, 1950.
- 20) HERLANT, M., *Ann. Endocr.*, **14**, 64, 1953.
- 21) HERLANT, M., *C. R. Soc. belge Biol.*, **147**, 528, 1953.
- 22) JAYLER and KNOWLTON, *J. clin. Invest.*, **29**, 1430, 1950.
- 23) JAYLER, W., *Clinical ACTH*, vol. **1**, 77, 1951.
- 24) TARANTINO, C., *Folia endocr.*, **4**, 197, 1951.
- 25) NELSON et al., *Science*, **119**, 379, 1953.
- 26) BORNSTEIN and TREWELLA, *Lancet*, **2**, 678, 1950.
- 27) PARROT, D. M. V., *J. Endocr.*, **7**, lxxx, 1951.
- 28) ASTWOOD et al., *J. Amer. chem. Soc.*, **73**, 2969, 1951.
- 29) SYDNOR et al., *J. Endocr. and Metabolism*, **13**, 891, 1953.
- 30) GREENSPAN et al., *Endocrinology*, **46**, 261, 1950.
- 31) SACKS, M. S., *Ann. intern. Med.*, **36**, 911, 1952.
- 32) NELSON et al., *Clinical ACTH*, vol. **1**, 49, 1951.
- 33) DOBRINER and LIEBERMAN, in GORDON, *Symposium on Steroid Hormones*, 1950, page 46.
- 34) JACOBSEN and PINCUS, *Amer. J. Med.*, **10**, 531, 1951.
- 35) MASON and ENGSTROM, *Physiol. Rev.*, **30**, 321, 1950.
- 36) THORN et al., *The Diagnosis and Treatment of Adrenal Insufficiency*, 2nd edition, Springfield, 1951.
- 37) FERRAZZINI, F., *Praxis*, **47**, 964, 1951.
- 38) MASON, H., *J. biol. Chem.*, **182**, 131, 1950.
- 39) SCHNEIDER, J., *J. biol. Chem.*, **183**, 365, 1950.
- 40) MASON and SPRAGUE, *J. biol. Chem.*, **175**, 451, 1948.
- 41) MASON, H., *Clinical ACTH*, 168, 1950.
- 42) SPRAGUE et al., *Arch. intern. Med.*, **85**, 199, 1950.
- 43) URIBE et al., *Amer. J. Dis. Child.*, **79**, 385, 1950.
- 44) PINCUS et al., *Endocrinology*, **8**, 221, 1948.
- 45) VENNING, E. H., in GORDON, *Symposium on Steroid Hormones*, 98, 1950.
- 46) DOBRINER et al., *Clinical ACTH*, vol. **1**, 65, 1951.
- 47) COOK and WHERRY, *Hum. Biol.*, **22**, 104, 1950.
- 48) PERRY and CHOCHINOW, *Canad. J. Res. (E)*, **28**, 47, 1950.
- 49) TALBOT et al., *Clinical ACTH*, vol. **1**, 20, 1951.
- 50) RANSOHOFF et al., *Clinical ACTH*, vol. **1**, 160, 1951.
- 51) WILLIAMS, H. R., *Amer. J. Med.*, **10**, 612, 1951.
- 52) THORN et al., *Trans. Ass. Amer. Phys.*, **62**, 233, 1949.
- 53) THORN et al., *Amer. J. Med.*, **10**, 595, 1951.
- 54) GORDON, E. B., *J. Lab. clin. Med.*, **36**, 827, 1950.
- 55) GORDON et al., *Clinical ACTH*, vol. **2**, 30, 1951.
- 56) QUERIDO et al., *Acta Endocr.*, **6**, 90, 1951.
- 57) RENOLD et al., *New Engl. J. Med.*, **244**, 796, 1951.
- 58) SAYERS et al., *Endocrinology*, **42**, 379, 1948.
- 59) ROCHE, M., *Clinical ACTH*, vol. **2**, 36, 1951.
- 60) PINCUS et al., *Clinical ACTH*, vol. **1**, 40, 1951.
- 61) CONN et al., *Science*, **113**, 713, 1951.
- 62) INGLE et al., *Anat. Rec.*, **71**, 363, 1938.
- 63) SAYERS, G., *Amer. J. Med.*, **10**, 539, 1951.
- 64) SAYERS, G., *J. clin. Endocr.*, **9**, 593, 1949.
- 65) DESAULLES et al., *Schweiz. med. Wschr.*, **83**, 1088, 1953.
- 66) VOGT, M., quoted by LONG¹⁰.
- 67) SAYERS and SAYERS, *Endocrinology*, **40**, 265, 1947.
- 68) CHENG et al., *Amer. J. Physiol.*, **158**, 45, 1949.
- 69) FORTIER and SELYE, *Amer. J. Physiol.*, **159**, 433, 1949.
- 70) RECANI et al., *Fed. Proc.*, **7**, 99, 1948.
- 71) UOTILA, U. U., *Endocrinology*, **25**, 605, 1939.
- 72) CHENG et al., *Amer. J. Physiol.*, **159**, 426, 1949.
- 73) SCHWEIZER and LONG, *Endocrinology*, **46**, 191, 1950.
- 74) BROUHA et al., *J. Physiol.*, **87**, 345, 1936.
- 75) RAY and CONSOLE, *Ann. Surg.*, **130**, 652, 1949.
- 76) TEPPERMAN and BOGARDUS, *Endocrinology*, **43**, 448, 1948.
- 77) TEPPERMAN and TEPPERMAN, *Ann. Rev. Physiol.*, **12**, 503, 1950.
- 78) SAYERS, G., *Recent Progr. Hormone Res.*, **2**, 81, 115, 1948.
- 79) ROCHE et al., *New Engl. J. Med.*, **242**, 307, 1950.
- 80) COLFER et al., *J. Physiol.*, **111**, 328, 1950.
- 81) DEGROOT and HARRIS, *J. Physiol.*, **111**, 335, 1950.
- 82) HUME and WITTENSTEIN, *Clinical ACTH*, 134, 1950.
- 83) HARRIS, G. W., *J. Physiol.*, **111**, 347, 1950.
- 84) MARKEE et al., *Endocrinology*, **38**, 345, 1946.
- 85) GERSHBERG et al., *Yale J. Biol. Med.*, **23**, 32, 1950.
- 86) FROST et al., *J. Lab. clin. Med.*, **38**, 523, 1951.
- 87) BROWNE, J. S. L., *Recent Progr. Hormone Res.*, **7**, 103, 1952.
- 88) RASMUSSEN, A. T., *Endocrinology*, **23**, 263, 1938.
- 89) HOUSSAY et al., *C. R. Soc. Biol.*, **120**, 725, 1935.
- 90) WISLOCKI and KING, *Amer. J. Anat.*, **58**, 421, 1936.
- 91) HARRIS, G. W., *Brit. med. J.*, **2**, 627, 1951.
- 92) GREEP and BARNETT, *Endocrinology*, **49**, 172, 1951.
- 93) TANG and PATTON, *Endocrinology*, **49**, 86, 1951.
- 94) FORTIER, C., *J. clin. Endocr.*, **11**, 751, 1951.
- 95) CORCORAN and PAGE, *J. Lab. clin. Med.*, **33**, 1326, 1948.
- 96) GODOWSKI, Z. Z., *Brit. med. J.*, **1**, 46, 1948.
- 97) HILLS et al., *Blood*, **3**, 755, 1948.
- 98) LONG and FRY, *Proc. Soc. exp. Biol.*, **59**, 67, 1945.
- 99) LOVE, W. D., *Proc. Soc. exp. Biol.*, **75**, 639, 1950.
- 100) PASCHKIS et al., *J. clin. Endocr.*, **9**, 658, 1949.
- 101) MARKEE et al., *Recent Progr. Hormone Res.*, **2**, 117, 1948.
- 102) MARKEE et al., *Recent Progr. Hormone Res.*, **7**, 139, 1952.
- 103) GRAY and MUNSON, *Endocrinology*, **48**, 471, 1951.
- 104) LAST et al., *Science*, **112**, 47, 1950.
- 105) VAN ARMAN, *Amer. J. Physiol.*, **164**, 476, 1951.
- 106) WILKINS et al., *Clinical ACTH*, vol. **2**, 81, 1951.
- 107) O'DONNELL et al., *Arch. intern. Med.*, **88**, 28, 1951.
- 108) SPRAGUE et al., *Clinical ACTH*, vol. **2**, 38, 1951.
- 109) FELDMANN, J., *Anat. Rec.*, **109**, 41, 1951.
- 110) GOLDEN et al., *Proc. Soc. exp. Biol.*, **74**, 455, 1950.
- 111) LAQUEUR, G. L., *Science*, **112**, 429, 1950.
- 112) PERERA et al., *J. clin. Invest.*, **29**, 735, 1950.
- 113) SZEGO and WHITE, *Fed. Proc.*, **8**, 153, 1949.
- 114) EDELMAN et al., *Clinical ACTH*, vol. **2**, 332, 1951.
- 115) HILL et al., *J. clin. Endocr.*, **10**, 1375, 1950.
- 116) SOFFER et al., *Proc. Soc. exp. Biol.*, **71**, 117, 1949.
- 117) SOFFER et al., *Proc. Soc. exp. Biol.*, **76**, 763, 1951.
- 118) VAN MIDDLESWORTH, *Fed. Proc.*, **10**, 140, 1951.
- 119) WOLFSON et al., *Clinical ACTH*, vol. **2**, 95, 1951.
- 120) THORN et al., *Clinical ACTH*, vol. **2**, 117, 1951.
- 121) ENGEL, F. L., *Amer. J. Med.*, **10**, 556, 1951.
- 122) INGLE, D. J., in GORDON, *Symposium on Steroid Hormones*, 150, 1950.
- 123) SELYE, H., *Stress*, Montreal, 1950.
- 124) VENNING and BROWNE, *Ann. N. Y. Acad. Sci.*, **50**, 627, 1949.
- 125) LEGER et al., *Proc. Soc. exp. Biol.*, **69**, 529, 1948.
- 126) INGLE et al., *Amer. J. Physiol.*, **157**, 99, 1949.
- 127) TOBIAN and STRAUSS, *Proc. Soc. exp. Biol.*, **69**, 529, 1948.
- 128) ENGEL, F. L., *Clinical ACTH*, vol. **1**, 235, 1951.
- 129) HERLANT, M., *Proc. Soc. exp. Biol.*, **73**, 399, 1950.
- 130) INGLE et al., *Amer. J. Physiol.*, **149**, 510, 1947.
- 131) SELYE and DOSNE, *Proc. Soc. exp. Biol.*, **71**, 117, 1949.
- 132) INGLE, D. J., *Ann. intern. Med.*, **35**, 652, 1951.
- 133) SELYE, H., *Clinical ACTH*, vol. **2**, 24, 1951.
- 134) ENGEL, F. L., *Endocrinology*, **45**, 170, 1949.
- 135) ENGEL, F. L., *Recent Progr. Hormone Res.*, **6**, 1951.
- 136) WHITNEY and BENNETT, *Fed. Proc.*, **9**, 134, 1950.
- 137) LLOYD, C. W., *Recent Progr. Hormone Res.*, **7**, 469, 1952.
- 138) SPIERS and MAYER, *Endocrinology*, **45**, 403, 1949.
- 139) HECHTER, O., *Endocrinology*, **42**, 285, 1948.
- 140) COREY and BRITTON, *Amer. J. Physiol.*, **131**, 783, 1941.
- 141) BAKER, B. L., *Recent Progr. Hormone Res.*, **7**, 331, 1952.
- 142) BAKER et al., *Amer. J. Anat.*, **88**, 313, 1951.
- 143) DOUGHERTY and WHITE, *Endocrinology*, **35**, 1, 1944.
- 144) TALBOT, N. B., *Pediatrics*, **6**, 1, 1950.
- 145) INGLE, D. J., *Ann. N. Y. Acad. Sci.*, **50**, 576, 1949.
- 146) SAYERS, G., *Physiol. Rev.*, **30**, 244, 1950.
- 147) CONN et al., *Clinical ACTH*, vol. **1**, 221, 1951.
- 148) BURTON et al., *J. clin. Endocr.*, **13**, 48, 1953.

Bibliography (continued)

- 149) AMELUNG et al., *Klin. Wschr.*, **31**, 386, 1953.
- 150) AMELUNG et al., *J. clin. Endocr.*, **13**, 1125, 1953.
- 151) BOLAND and HEADLEY, *J. Amer. med. Ass.*, **145**, 8, 1951.
- 152) BOLAND, E. W., *ibid.*, **150**, 1281, 1952.
- 153) WARD et al., *Proc. Mayo Clin.*, **26**, 361, 1951.
- 154) STANBURY, S. W., *Lancet*, **2**, 664, 1951.
- 155) BORDEN et al., *Fed. Proc.*, **10**, 376, 1951.
- 156) KLEIN, R., *J. clin. Invest.*, **30**, 318, 1951.
- 157) ELIEL et al., *Clinical ACTH*, vol. **1**, 196, 1951.
- 158) BRUST et al., *Clinical ACTH*, vol. **1**, 177, 1951.
- 159) SPRAGUE, R. G., *Amer. J. Med.*, **10**, 567, 1951.
- 160) BERGENSTAHL et al., *Clinical ACTH*, vol. **1**, 250, 1951.
- 161) PEARSON et al., *Cancer*, **2**, 943, 1949.
- 162) BENEDICT et al., *Fed. Proc.*, **9**, 149, 1950.
- 163) INGBAR et al., *Clinical ACTH*, vol. **1**, 130, 1951.
- 164) INGLE, D. J., *J. clin. Endocr.*, **10**, 1312, 1950.
- 165) BONGIOVANNI et al., *J. clin. Invest.*, **29**, 798, 1950.
- 166) FARNSWORTH and RUPPENTHAL, *J. Lab. clin. Med.*, **38**, 407, 1951.
- 167) HENCH et al., *Proc. Mayo Clin.*, **24**, 181, 1949.
- 168) BERNFELD et al., *Clinical ACTH*, vol. **1**, 282, 1951.
- 169) LONG et al., *Endocrinology*, **26**, 309, 1940.
- 170) CONN et al., *J. Lab. clin. Med.*, **33**, 651, 1948.
- 171) BROWNE et al., *J. clin. Endocr.*, **10**, 1363, 1950.
- 172) EARLE et al., *Clinical ACTH*, vol. **1**, 139, 1951.
- 173) KASS et al., *Proc. Soc. exp. Biol.*, **73**, 669, 1950.
- 174) MCQUARRIE et al., *Clinical ACTH*, vol. **2**, 69, 1951.
- 175) KUHN and HOLLDACK, *Dtsch. med. Wschr.*, **77**, 457, 1952.
- 176) LEVIN and FARBER, *Proc. Soc. exp. Biol.*, **74**, 758, 1950.
- 177) BAKER et al., *Anat. Rec.*, **102**, 313, 1948.
- 178) LI et al., *Arch. Biochem.*, **23**, 51, 1949.
- 179) BAKER et al., *Proc. Soc. exp. Biol.*, **73**, 337, 1950.
- 180) BAKER and INGLE, *Endocrinology*, **43**, 422, 1948.
- 181) KINSELL et al., *Clinical ACTH*, vol. **1**, 308, 1951.
- 182) DOUGHERTY and WHITE, *Amer. J. Anat.*, **77**, 81, 1945.
- 183) ASLING et al., *Endocrinology*, **48**, 534, 1951.
- 184) CASTOR and BAKER, *Endocrinology*, **47**, 234, 1950.
- 185) GRAY et al., *Proc. Soc. exp. Biol.*, **78**, 338, 1951.
- 186) JACKSON, C. M., *J. exp. Zool.*, **19**, 99, 1915.
- 187) JACKSON, C. M., *Amer. J. Anat.*, **18**, 75, 1915.
- 188) MACLENNAN and JACKSON, *Arch. Path.*, **15**, 636, 1933.
- 189) JÄRVINEN, K. A. J., *Brit. med. J.*, **2**, 1377, 1951.
- 190) DOUGHERTY, T. F., *Pituitary-Adrenal Function, Amer. Ass. for the Advancement of Science*, 1951.
- 191) DOUGHERTY and SCHNEEBELY, *Proc. Soc. exp. Biol.*, **75**, 854, 1950.
- 192) KALLOS, P., *Progress in Allergy*, vol. III, Basel, 1952.
- 193) FISHEL, E. E., *Bull. N. Y. Acad. Med.*, **26**, 255, 1950.
- 194) BJØRNBOE et al., *J. exp. Med.*, **93**, 37, 1951.
- 195) GERMUTH et al., *J. exp. Med.*, **94**, 139, 1951.
- 196) FISHEL et al., *Proc. Soc. exp. Biol.*, **77**, 111, 1951.
- 197) LEITH et al., *J. Allergy*, **22**, 99, 1951.
- 198) ROSE, B., *Ann. Rev. Med.*, **2**, 155, 1951.
- 199) ROSE, B., *Recent Progr. Hormone Res.*, **7**, 375, 1952.
- 200) LONG and FAVOUR, *Bull. Johns Hopk. Hosp.*, **87**, 186, 1950.
- 201) LONG and MILES, *Lancet*, **1**, 492, 1950.
- 202) HAVENS et al., *Fed. Proc.*, **10**, 410, 1951.
- 203) THORN et al., *New Engl. J. Med.*, **248**, 232, 284, 323, 369, 414, 588, 632, 1953.
- 204) HENCH et al., *J. Amer. med. Ass.*, **144**, 1327, 1950.
- 205) HOLBROOK et al., *Clinical ACTH*, vol. **2**, 599, 1951.
- 206) STEINBROCKER et al., *Bull. N. Y. Acad. Med.*, **27**, 560, 1951.
- 207) POLLEY et al., *J. Lab. clin. Med.*, **38**, 937, 1951.
- 208) HENCH, P. S., paper read at 8th Int. Congress of Rheumatic Diseases, Geneva, 1953.
- 209) BARRIT and STUMPE, *Amer. J. med. Sci.*, **22**, 3, 1951.
- 210) GORDON et al., *Clinical ACTH*, vol. **2**, 457, 1951.
- 211) STEFFENSON, E. H., *J. Amer. med. Ass.*, **150**, 1660, 1952.
- 212) LAVAL, J., *Arch. Ophtal.*, **50**, 299, 1953.
- 213) TUCKER et al., *Clinical ACTH*, vol. **2**, 696, 1951.
- 214) SOFFER and BADER, *J. Amer. med. Ass.*, **149**, 1002, 1952.
- 215) DUBOIS et al., *J. Amer. med. Ass.*, **149**, 995, 1952.
- 216) KIERLAND et al., *J. Amer. med. Ass.*, **148**, 23, 1952.
- 217) SOFFER et al., *Clinical ACTH*, vol. **2**, 680, 1951.
- 218) BARNES et al., *Amer. J. Dis. Child.*, **82**, 397, 1951.
- 219) DORFMAN et al., *Clinical ACTH*, vol. **2**, 645, 1951.
- 220) WILSON et al., *Clinical ACTH*, vol. **2**, 627, 1951.
- 221) ROCHE et al., *Clinical ACTH*, vol. **2**, 373, 1951.
- 222) DURAND and RENOUX, *Sem. Hôp. Paris*, **29**, 2555, 1953.
- 223) ADAMS et al., *Clinical ACTH*, vol. **2**, 322, 1951.
- 224) ADAMS et al., *J. Amer. med. Ass.*, **146**, 31, 1951.
- 225) HUME et al., *Clinical ACTH*, vol. **2**, 281, 1951.
- 226) MUNSON et al., *Fed. Proc.*, **9**, 208, 1950.
- 227) WHITELAW, M. J., *Clinical ACTH*, vol. **2**, 310, 1951.
- 228) LEVITT, S., *Brit. med. J.*, **1**, 541, 1954.
- 229) CLUXTON, H. E., *Clinical ACTH*, vol. **2**, 445, 1951.
- 230) THORPE, E., *Clinical ACTH*, vol. **2**, 340, 1951.
- 231) SUZMAN and RUDOLPH, *Lancet*, **1**, 660, 1951.
- 232) LUONGO et al., *New Engl. J. Med.*, **245**, 757, 1951.
- 233) NICKEL, R. W., *Amer. Arch. Dermatol.*, **64**, 372, 1951.
- 234) KINSELL, L. W., *Ann. intern. Med.*, **35**, 615, 1951.
- 235) EVANS and RAKEMAN, *Arch. intern. Med.*, **90**, 96, 1952.
- 236) BUTTERFIELD et al., *Lancet*, **1**, 737, 1952.
- 237) FARBER et al., *Clinical ACTH*, vol. **2**, 251, 1951.
- 238) PEARSON et al., *Bull. N. Y. Acad. Med.*, **26**, 235, 1950.
- 239) BETHELL et al., *Clinical ACTH*, vol. **2**, 173, 1951.
- 240) BETHELL et al., *Trans. Ass. Amer. Phys.*, **64**, 199, 1951.
- 241) HILL et al., *Clinical ACTH*, vol. **2**, 181, 1951.
- 242) WILKINS et al., *J. clin. Endocr.*, **12**, 257, 1952.
- 243) WILKINS et al., *J. clin. Endocr.*, **12**, 277, 1952.
- 244) WILKINS et al., *J. clin. Endocr.*, **12**, 1015, 1952.
- 245) HOWARD, E., *Clinical ACTH*, vol. **1**, 327, 1951.
- 246) KINSELL, L. W., *Ann. intern. Med.*, **35**, 615, 1951.
- 247) HUME et al., *Clinical ACTH*, vol. **2**, 281, 1951.
- 248) SALASSA et al., *J. Amer. med. Ass.*, **152**, 1509, 1953.
- 249) KIRKPATRICK, *Lancet*, **2**, 54, 1951.
- 250) CONN et al., unpublished, quoted by HAYNES, W. J., *Recent Progr. Hormone Res.*, **7**, 255, 1952.
- 251) See THORN et al.²⁰³, p. 632, 1953.
- 252) THORN and FORSHAM, *Recent Progr. Hormone Res.*, **4**, 229, 1949.
- 253) MAQSOOD, M. J., *J. Endocr.*, **7**, 82, 1950.
- 254) MUNSON and BRIGGS, *Recent Progr. Hormone Res.*, **11**, 83, 1955.
- 255) SIMPSON and TAIT, *Recent Progr. Hormone Res.*, **11**, 183, 1955.

Clinical ACTH, 1950 (1951) = Proceedings of the First (Second) Clinical ACTH Conference, 1950 (1951).

Growth hormone (Somatotropic hormone, STH)

Chemistry

As prepared by the methods so far in use¹⁻³, STH consists of a protein of molecular weight 46,800 and isoelectric point pH 6.85^{1,4}. More recently it has been prepared by the oxycellulose technique of ASTRWOOD⁵. It has not yet been possible to decide whether this protein is actually the growth hormone or whether the latter is a compound intimately combined with the protein.

Site of formation

Acidophil cells of the anterior pituitary.

Physiology and Function

STH has so far been prepared only from the pituitary of cattle and pigs, and its growth-promoting activity has been demonstrated only on rats. Deductions from the presently available data should therefore be made with reserve, particularly in view of the fact that no significant effects on the human organism have yet been demonstrated with the available preparations⁶. It is nevertheless certain that a pituitary growth factor, i.e. a metabolic hormone with properties analogous to those of the growth hormone, must be present in man. It remains to be demonstrated, however, that this growth factor is identical with the growth hormone.

The overall effect of STH on metabolism is in the general direction of that pertaining in hunger and during growth: inhibition of breakdown of proteins, principally, and of sugars to a lesser degree, accompanied by an absolute or relative increase in oxidation of fats⁷. Since protein-, fat- and sugar-metabolism are closely interconnected and are regulated by a number of mutually interacting hormones, it is extremely difficult to establish what the primary effects of the individual hormones are. The effects now attributed to a particular hormone may later be found to be due to another hormone the action of which is only made possible or conditioned by the first hormone (permissive reaction). According to the metabolic state an effect can also change markedly or even be reversed, to which must be added the differing modes of action in different species. In the light of these circumstances apparently contradictory observations, such as the simultaneous synergistic and antagonistic effects of STH and insulin on the same substrate, become explicable.

The effects of STH are summarized in the following table (after YOUNG⁸) in the order of their discovery:

Effect	Experimental animal or tissue	Authors
1. Growth-promotion	Hypophysectomized rats	LI et al. ¹ , 1945
2. Diabetogenic effect	Cats	COTES et al. ⁹ , 1949
3. Galactogenic effect	Cows	COTES et al. ¹⁰ , 1949
4. Inhibition of muscle-sugar breakdown	Hypophysectomized rats	RUSSELL and WILHELM ¹¹ , 1950
5. Insulin antagonist	Hypophysectomized dog	DE BODO et al. ¹² , 1950
6. Stimulation of insulin secretion	Cats	MILMAN et al. ¹³ , 1951
7. Stimulation of secretion of the pancreatic hyperglycaemic factor (glucagone)	Cats	BORNSTEIN et al. ¹⁴ , 1951
8. Promotion of insulin action	Rat diaphragm	OTTAWAY ¹⁵ , 1951; PARK et al. ¹⁶ , 1952
9. Improvement of water diuresis	Hypophysectomized dog	DE BODO et al. ¹⁷ , 1951
10. Inhibition of fat synthesis from acetates	Liver slices (cats)	BRADY et al. ¹⁸ , 1951
11. Lowering of the respiratory quotient	Rat diaphragm	RECANT ¹⁹ , 1952

Growth-promoting effect. The growth-promoting effect of STH is explicable from its general effect on metabolism. It promotes protein synthesis, an effect characterized by an increase in the protein content of the tissues accompanied by a simultaneous decrease in fat content, lowering of the blood amino-acid level and retention of nitrogen (lowered N-elimination). It also promotes the epiphyseal cartilage development while at the same time increasing the phosphatase and inorganic phosphate concentration of the blood. The growth-promoting effect of STH only occurs when sufficient insulin is available.

Sugar metabolism, diabetogenic effect. STH retards the sugar uptake of muscle and thus brings about an increase in blood sugar. In certain circumstances it can also cause a lowering of the blood sugar²⁰⁻²² and an increase in muscle sugar uptake^{15,16}. It can therefore be either an antagonist or synergist of insulin, according to the metabolic situation. Through its peripheral diabetogenic effect STH stimulates insulin secretion. Simultaneously the glucagone secretion of the pancreas is also stimulated, very probably as a direct effect of STH. Prolonged administration of STH to adult animals leads to persistent diabetes with pathological changes of the LANGERHANS islets. This effect does not occur with suckling or young growing animals⁸.

The diabetes provoked by STH is insulin-resistant and differs from "normal" human diabetes, in which the elimination of N, Na and K as well as of sugar is increased, in that the elimination of these elements is decreased²³. An interesting discovery²⁴ of possible future clinical use is that diabetes, insulin resistance and toxic manifestations following prolonged administration of large doses of STH can be prevented by simultaneous administration of hydrocortisone or cortisone.

Since hydrocortisone and cortisone also have a diabetogenic effect it is appropriate to summarize the differences between these hormones and STH:

1. STH acts diabetogenically through inhibition of the muscle sugar uptake (myoglycostatically) and by retarding the action of insulin in the cell.
2. Hydrocortisone and cortisone also inhibit muscle sugar uptake, but in addition cause an increase of glycogenolysis in liver and muscle as well as an increase in glyconeogenesis. STH has no effect on glycogenolysis but inhibits glyconeogenesis.
3. The diabetogenic effect of hydrocortisone and cortisone is markedly weaker than that of STH and is short-lived and reversible. That of STH lasts longer, is often irreversible, and is markedly stronger than that of hydrocortisone.

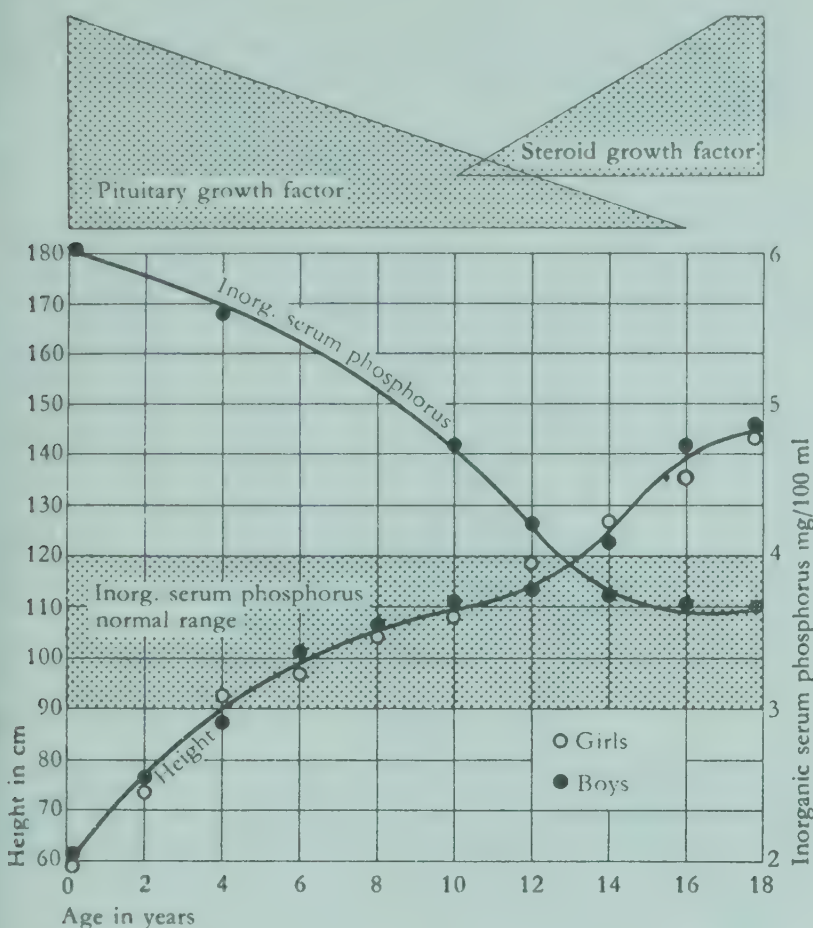
The following "classification" illustrates the respective roles of adrenaline, hydrocortisone and STH as antagonists of insulin in sugar metabolism²⁴:

1. Adrenaline does not appear to be indispensable to normal sugar metabolism, although it may perhaps have a certain significance in conditions of stress (reinforcement of the action of hydrocortisone due to its qualitatively very similar effect on sugar metabolism).
2. Hydrocortisone and cortisone are indispensable to normal sugar metabolism, which is furthermore possible in the absence of STH provided these adrenocortical hormones are available. Without them sugar metabolism is only possible when sufficient exogenous sugar is administered (absence of glyconeogenesis) although its level can in no respect be considered as normal.
3. STH lowers the sensitivity to insulin but, together with insulin, cannot maintain sugar metabolism in the absence of adrenocortical hormones.

Clinical significance

As already mentioned, it has not yet been possible to reproduce in man the effects of STH observed in animals. On the other hand there is a great deal of clinical evidence for the existence of a hormone with analogous activity.

Growth. Human growth takes place in two distinct successive phases, influenced respectively by the pituitary growth factor and the sex hormones (see diagram).



(Modified after KINSELL, L. W., *J. clin. Endocr.*, 8, 1013, 1948)

Pituitary dwarfism results not only from deficiency of STH but also from hypofunction of the whole pituitary. Panhypopituitary dwarfs are characterized by bodily proportions resembling those of a child and retained throughout life. The ossification centres appear late, the epiphyses often fail to unite even in maturity. In addition to marked sexual infantilism (minimal development of genitals and breasts, complete absence of sexual hair) other noticeable characteristics are the small hands and feet, the close proximity of the fingers, and the soft silky texture of the hair of the head. The skin becomes dry and wrinkled relatively early in adolescence, giving such dwarfs a withered owlish appearance often so marked that they are thought to be prematurely senile (VARIOT's *nanisme sénile*²⁵, GILFORD's *progeria*²⁶). The LORAIN-LEVY syndrome is also a form of pituitary dwarfism and is frequently caused by a cranial pharyngioma. From the point of view of differential diagnosis genetical dwarfism (primordial dwarfs with normal union of the epiphyses and normal sexual function), chondrodystrophic dwarfism, and dwarfism due to hypofunction of thyroid, gonads, etc. must be distinguished from pituitary dwarfism.

Overproduction of STH during youth (before the union of the epiphyses) results in pituitary gigantism. After the union of the epiphyses it results in acromegaly. Hyperproduction of STH may be due to a hyperplasia, an adenoma, or more rarely a carcinoma of the acidophil cells.

Pituitary gigantism. Arm-spread usually greater than body length, bone structure and musculature well-developed, splanchnomegaly. Union of the epiphyses is delayed. Somatic, sexual and metabolic disturbances to a varying degree. The libido can be above or below normal. When the over-production of STH in pituitary giants continues beyond puberty acromegalic symptoms also develop. Pituitary gigantism is often difficult to distinguish diagnostically from genetical gigantism but is easily distinguishable from eunuchoidal gigantism.

Acromegaly. Enlargement and distortion of the distal bone parts, noticeable primarily in the hands, feet and face, and kyphoscoliosis, usually permitting immediate visual diagnosis. It is often accompanied by hyperthyreosis and diabetes mellitus, as well as hypertonia, hypertrichosis and galactorrhoea.

Diabetes. The fact that STH as well as hydrocortisone and cortisone (or ACTH) are antagonistic to insulin, and that overproduction of STH and/or hydrocortisone (or ACTH) must therefore result in compensatory over-production of insulin, may perhaps throw some light on certain cases of diabetes. Thus acromegaly is often accompanied by an insulin-resistant diabetes more severe than the diabetes which often occurs in CUSHING's syndrome. This is in agreement with the experimental observations already mentioned²⁷. The fact that the majority of diabetic children are taller and physically better developed at the onset of diabetes than normal children of the same age points in the same direction²⁸, as does also the tendency to diabetes of mothers (if they are not already diabetic) of children of excessive size at birth²⁹.

Adiposity. The relation STH/adrenocortical hormones/insulin also appears to play a part in the aetiology of adiposity. It is well known that fat children are usually taller than average. CUSHING³⁰ in 1912 described an extreme example of this kind: an acromegalic giant was at birth the size of a one year old child and was extraordinarily adipose in the first year of its life. The frequently observed concomitance of diabetes and adiposity is likewise in keeping with this view, as is the experimentally established fact³¹ that STH administered to experimental animals brings about an increase in weight which is not observed in control animals with quantitatively and qualitatively the same food intake. On the other hand it must not be overlooked that the increased STH/hydrocortisone/insulin production can be explained as secondary result of a psychically-conditioned polyphagia, as indeed it probably is in most cases³².

Therapeutic application

In pituitary dwarfism, experimentally, provided that union of the epiphyses has not taken place. In hyperinsulinism, experimentally. STH sometimes produces toxic or allergic phenomena which can, however, be avoided by administration of hydrocortisone or cortisone.

Bibliography (for reviews see 7 and 8)

- ¹) LI et al., *J. biol. Chem.*, **159**, 353, 1945. ²) FISHMAN et al., *Science*, **106**, 402, 1947. ³) WILHELM et al., *J. biol. Chem.*, **176**, 735, 1948. ⁴) FRANKLIN et al., *J. biol. Chem.*, **169**, 515, 1947. ⁵) ASTWOOD et al., *J. Amer. chem. Soc.*, **73**, 2969, 1951. ⁶) Report of discussion on 7. ⁷) YOUNG, F. G., *Recent Progr. Hormone Res.*, **8**, 471, 1953. ⁸) YOUNG, F. G., *Exposés annuels de biochimie médicale*, Paris, 1953. ⁹) COTES et al., *Nature*, **164**, 209, 1949. ¹⁰) COTES et al., *Nature*, **164**, 992, 1949. ¹¹) RUSSELL and WILHELM, *Endocrinology*, **47**, 26, 1950. ¹²) DE BODO et al., *Amer. J. Physiol.*, **163**, 310, 1950. ¹³) MILMAN et al., *Amer. J. Physiol.*, **166**, 354, 1951. ¹⁴) BORNSTEIN et al., *Nature*, **168**, 903, 1951. ¹⁵) OTTAWAY, J. H., *Nature*, **167**, 1064, 1951. ¹⁶) PARK et al., *J. biol. Chem.*, **197**, 151, 1952. ¹⁷) DE BODO et al., *Proc. Soc. exp. Biol. N. Y.*, **76**, 612, 1951. ¹⁸) BRADY et al., *J. biol. Chem.*, **193**, 459, 1951. ¹⁹) RECENT, L., *Fed. Proc.*, **11**, 272, 1952. ²⁰) SCOTT and ENGEL, *Endocrinology*, **46**, 582, 1950. ²¹) MILMAN and RUSSELL, *Endocrinology*, **47**, 114, 1950. ²²) KURTZ et al., *Proc. Soc. exp. Biol.*, **76**, 21, 1951. ²³) BENNET and LI, *Amer. J. Physiol.*, **150**, 400, 1947. ²⁴) DE BODO and SINKOFF, *Recent Progr. Hormone Res.*, **8**, 511, 1953. ²⁵) SAINTON et al., *Endocrinologie clinique, thérapeutique et expérimentale*, Paris, 1942. ²⁶) GILFORD, H., *The Disorders of Postural Growth and Development*, 1911. ²⁷) CAMPBELL et al., *Endocrinology*, **46**, 273, 1950. ²⁸) COGGESHALL and ROOT, *Endocrinology*, **26**, 1, 1940. ²⁹) MILLER et al., *J. Amer. med. Ass.*, **124**, 271, 1944. ³⁰) CUSHING, H., *The Pituitary Body and his Disorders*, Philadelphia, 1912. ³¹) YOUNG, F. G., *Brit. med. J.*, **2**, 1167, 1951. ³²) MIRSKY, I. A., *Recent Progr. Hormone Res.*, **7**, 437, 1952.

Hormones of the posterior pituitary

Two posterior pituitary hormones have so far been identified, vasopressin and oxytocin. The chemical constitution of both as polypeptides has been established, and that of oxytocin confirmed by synthesis. This is the first time in the history of endocrinology that a hormone formerly thought to be a protein has been shown to be a peptide and its structure elucidated. There is a species difference between the structure of vasopressin obtained from hog and beef pituitaries, but none in the case of oxytocin.

Physiologically these two hormones are linked to one protein molecule¹⁻⁵ in which the properties of the two hormones are combined. One could therefore speak of one single posterior pituitary hormone and regard vasopressin and oxytocin as its active principles. This protein-hormone has a molecular weight between 20,000 and 30,000 and an isoelectric point of pH 4.8^{3,5}.

Dry posterior pituitary preparations contain vasopressin and oxytocin in the proportions of ca. 8:1. Total posterior pituitary preparations therefore exhibit predominantly the antidiuretic effect of vasopressin.

Sites of formation

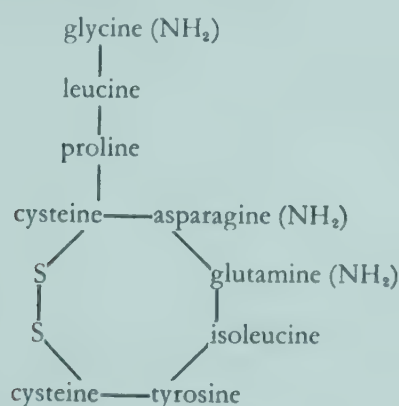
The posterior pituitary hormones originate most probably in the large-celled hypothalamus nuclei⁶. The neuropituitary is accordingly merely the storage organ for these hormones.

Physiology and Function (total posterior pituitary preparations)

Posterior pituitary preparations exhibit primarily a strong and rapid antidiuretic action (due to vasopressin) giving place in about one hour to an increased diuresis (due to oxytocin). In addition an action on the smooth musculature is apparent. Up to the present the only effect proved to be a physiological function is that on the uterus and mammary glands; all other effects, such as the stimulation of the intestinal and bladder musculature, increase in blood pressure, vasoconstriction, slowing of the heart-beat and lowering of the minute-volume, appear to be pharmacological effects.

Oxytocin

The determination of the structure of oxytocin by TUPPY⁷ and DU VIGNEAUD et al.^{8,9}, and its synthesis by the latter¹⁰, represent a milestone in the progress of hormone research. It is a nonapeptide of the following structural formula:



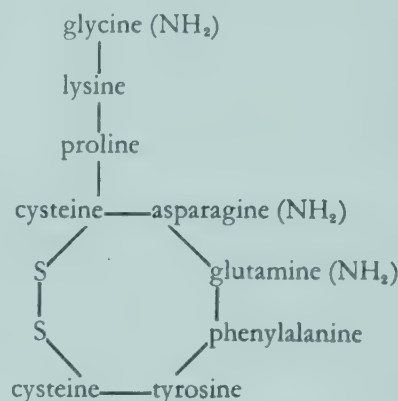
The effects of oxytocin are: 1. Contractional effect on the smooth musculature; the uterus (shortly before delivery) is most sensitive to this effect, followed by the intestine; appropriate doses result in milk-ejection from the mammary glands; 2. Diuretic effect on the kidneys.

It is questionable whether the effect on the smooth musculature is physiological (see above). The effect on the uterus on the other

hand is a purely hormonal effect, although in contradiction to this stands the fact that childbirth can take place when the pituitary is extirpated: this is explicable on the ground that the foetus and/or placenta store oxytocin and can thus act as substitutes for the pituitary. – The uterus reacts during pregnancy either not at all or only under certain circumstances; the sensitivity to oxytocin increases as pregnancy proceeds and is at a maximum immediately before parturition.

Vasopressin

DU VIGNEAUD et al.¹⁰ and ACHER and CHAUVET¹¹ have shown that hog vasopressin has the following structure:



Beef vasopressin¹² has a similar structure, with lysine replaced by arginine. Synthesis of a compound with this structure by DU VIGNEAUD et al. has yielded a product with biological activity closely resembling that of natural beef vasopressin.

Since vasopressin exhibits two effects, vasoconstriction and antidiuretic effect (adiuretin) it is regarded by some workers as a mixture of two hormones. It has not yet been possible, however, to separate the two factors, and it is doubtful whether the vasoconstrictive effect is a physiological effect. Confirmation of the above structure would provide proof that the two effects are exercised through a single chemical compound.

Vasopressin acts directly on the kidneys: 1. Antidiuretically (decreased water elimination); 2. Inhibiting filtration (increased salt elimination). The liberation of the hormone is regulated by the water content of the body. In prolonged thirsting the vasopressin concentration in the blood increases to such an extent that the hormone is eliminated in the urine, where it cannot normally be detected.

The adrenal cortex acts antagonistically, as has been indisputably demonstrated: its hormones act diuretically and cause polyuria in the absence of the inhibiting effect of the posterior pituitary. If now the anterior pituitary is extirpated the resulting lack of ACTH causes atrophy of the adrenal cortex and thereby cessation of the polyuria.

Larger doses result in the following symptoms: vasoconstriction of the peripheral blood vessels, slowing of the heart-beat and lowering of the minute-volume, increase in blood pressure – as with adrenaline, but by a different mechanism since ergotamine and ergotoxin, for example, have no effect on the action of vasopressin.

Therapeutic application

Total posterior pituitary preparations: diabetes insipidus; *vasopressin*: as for total preparations; *oxytocin*: primary and secondary insufficiency of labour pains, atonic uterine bleeding, post-operative paralysis of the intestines and bladder.

Bibliography (for reviews of physiology and function see ¹³⁻¹⁵)

- ¹) ABEL et al., *J. Pharmacol.*, **22**, 289, 1924. ²) ABEL, J. J., *J. Pharmacol.*, **40**, 139, 1930. ³) MACARTHUR, C. G., *Science*, **73**, 448, 1931. ⁴) ROSENFELD, M., *Bull. Johns Hopk. Hosp.*, **66**, 389, 1940. ⁵) VAN DYKE et al., *J. Pharmacol.*, **74**, 190, 1942. ⁶) HILD and ZETLER, *Pflügers Arch. ges. Physiol.*, **257**, 169, 1953. ⁷) TUPPY, H., *Biochim. biophys. Acta*, **11**, 449, 1953. ⁸) DU VIGNEAUD et al., *J. Amer. chem. Soc.*, **75**, 4879, 1953. ⁹) DU VIGNEAUD et al., *J. biol. Chem.*, **205**, 949, 1953. ¹⁰) DU VIGNEAUD et al., *J. Amer. chem. Soc.*, **75**, 4880, 1953. ¹¹) ACHER and CHAUVET, *Biochim. biophys. Acta*, **12**, 487, 1953. ¹²) DU VIGNEAUD et al., *J. Amer. chem. Soc.*, **74**, 3713, 1952. ¹³) STEHLE, R. L., *Vitam. and Horm.*, **7**, 1949, and **8**, 1950. ¹⁴) GAUNT and BIRNIE, *Hormones and Body Water*, Springfield, 1951. ¹⁵) VAN DYKE et al., *Recent Progr. Hormone Res.*, **11**, 1, 1955. ¹⁶) DU VIGNEAUD et al., *J. Amer. chem. Soc.*, **76**, 3115, 1954.

Steroid hormones

Chemistry

Nomenclature

The sex hormones and adrenocortical hormones belong to the group of compounds known as steroids. The skeleton of the steroid molecule consists of three six-membered rings A, B and C and a five-membered ring D (fig. 1), with methyl groups at positions C₁₀ and C₁₃. In the oestrogens the methyl group at C₁₀ is lacking and the ring A is aromatic (fig. 2).

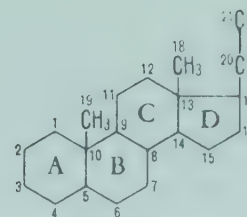


Fig. 1

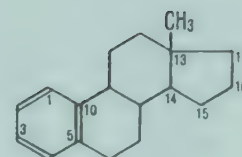


Fig. 2

Steroids with 2 methyl groups

The steroids with 2 methyl groups may be divided into two characteristic series according to the total number of carbon atoms in the molecule:

"C₁₉-steroids" have no side-chain at C₁₇: among these are testosterone and its metabolites (androgens). See figure 3.

"C₂₁-steroids" have a side-chain with 2 C-atoms at C₁₇: among these are progesterone and the adrenocortical hormones. See figure 4.

"C₂₄-steroids" have a branched side-chain with 5 C-atoms at C₁₇: this is characteristic of the bile acids. See figure 5.

"C₂₇-steroids" have a branched side-chain with 8 C-atoms at C₁₇: among these are cholesterol and the precursors of vitamin-D₃. See figure 6.

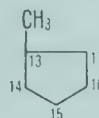


Fig. 3

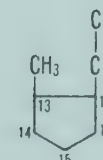


Fig. 4

Stereochemical designations

Since the biological activity of many hormones is markedly dependent on the stereochemical configuration, precise designation in this respect is necessary. In the following text the symbols α and β will be used to designate those forms in which certain substituents stand in *trans*- or *cis*-relationship respectively to the methyl groups at C₁₀ or C₁₃ as reference points. The *cis*-configuration indicates one in which the substituent is located spatially on the same side of the plane of the ring system as the reference group, the *trans*-configuration one in which the two groups are on different sides of this plane. In the structural formulae shown the *cis*(β)-position will be indicated by a full line and the *trans*(α)-position by a broken line (see fig. 7). The methyl group at C₁₀ is arbitrarily regarded as being situated *above* the plane of the ring. In the steroids the configuration of the methyl group at C₁₃, which serves as reference group, is with very few exceptions the same as that of the methyl group at C₁₀.

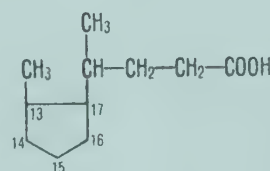


Fig. 5

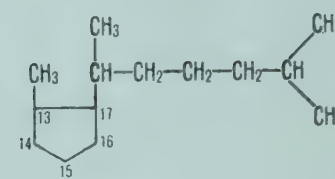


Fig. 6

Chemical structure

The structural formulae are given in the section which follows, "Metabolism of the Steroids".

Grouping

The steroids are grouped partly according to their chemical properties, partly according to their physiological characteristics, and partly according to their sites of formation in the body. There are no simple relationships between the groups and a hard and fast distinction is only possible on the basis of chemical structure (cf. the following page and nomenclature above).

Metabolism of the steroids

The parent substance of the steroids is cholesterol (see fig. 8) which can be synthesized endogenously from acetates. The adrenal cortex is one of the main sites of formation of cholesterol. Whether the sexual glands likewise build their hormones from acetates, from cholesterol, or from precursors synthesized in the adrenal cortex, is unknown. The current view of the degradation and urinary elimination of steroids is shown diagrammatically on pages 197-199.

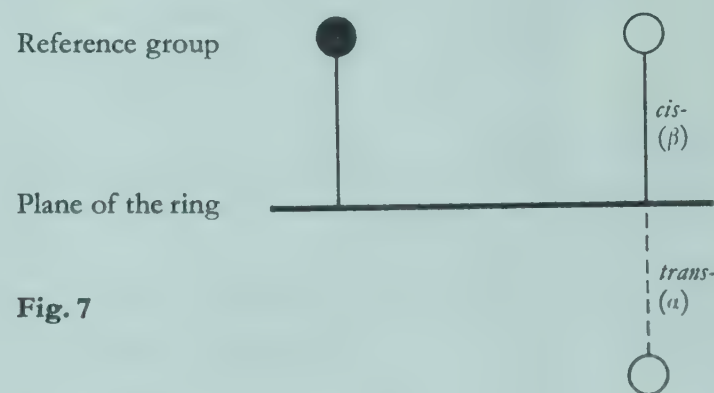
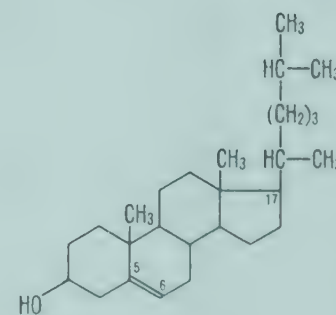


Fig. 7

Fig. 8

Cholesterol



Bibliography (chemistry and metabolism)

Chemical structure: FIESER and FIESER, *The Chemistry of Natural Products Related to Phenanthrene*, New York, 1949. FIESER, F. L., Review of the Chemistry of Steroids, in GORDON, *Symposium on Steroid Hormones*, 1950, page 14. SHOPPEE, C. W., Steroid Configuration, in *Vitam. and Horm.*, **8**, 255, 1950. (Aldosterone:) SIMPSON, TAIT, WETTSTEIN, NEHER, VON EUW, SCHINDLER and REICHSTEIN, *Experientia*, **10**, 132, 1954.

Metabolism: Steroid Metabolism and Estimation, *Ciba Foundation Colloquia on Endocrinology*, **2**, London, 1952. DOBRINER and LIEBERMAN, Steroid Excretion in Health and Disease, *Recent Progr. Hormone Res.*, **3**, 71, 1949. DOBRINER and LIEBERMAN, The Metabolism of Steroid Hormones in Humans, in GORDON, *Symposium on Steroid Hormones*, 1950, page 46. DOREMAN, R. I., Neutral Steroid Hormone Metabolites, and HEARD et al., The Application of ¹⁴C to the Study of the Metabolism of the Sterols and Steroid Hormones, both in *Recent Progr. Hormone Res.*, **9**, 1954.

Nomenclature of the medically most important steroids

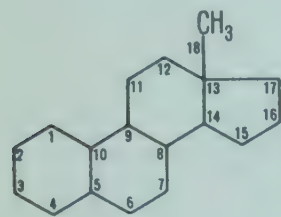
Legend: **Grotesque type, medium face**
Grotesque type, bold face
 Small type

= chemical designation¹
 = trivial name¹
 = synonyms¹

♀ = oestrogenic activity
 ♂ = androgenic activity
 ● = progestational activity

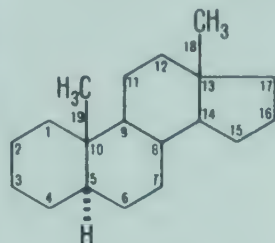
○ = adrenocortical-hormonal activity
 × = no hormonal activity
 ? = activity unknown

The chemical designations are derived from



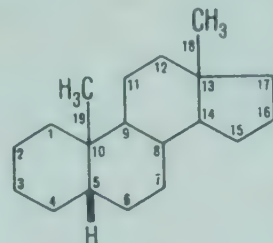
Oestrane :

The chemical designations are derived from



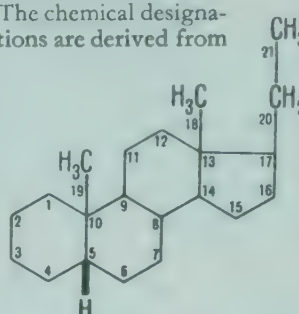
Androstane :

The chemical designations are derived from



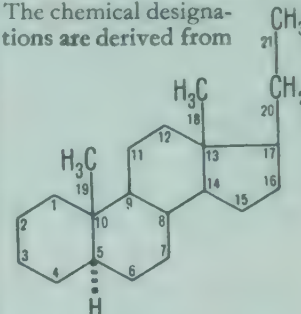
Aetiane³ :

The chemical designations are derived from



Pregnane :

The chemical designations are derived from



alloPregnane :

Occurring in the human organism

1:3:5(10)-Oestratriene-3:17β-diol
17β-Oestradiol, ♀²
 Dihydro-follicular hormone, dihydrotheelin, dihydro-folliculin, dihydromenformon, dihydroxyoestrin;
 (17β-form: *trans*-oestradiol, α-dihydroxyoestrin)

1:3:5(10)-Oestratrien-3β-ol-17-one
Oestrone, ♀
 α-Follicular hormone, menformon, theelin, ketohydroxyoestrin

1:3:5(10)-Oestratriene-3:17β:16α-triol
Oestriol, ♀
 Theelol, trihydroxyoestrin, follicular hormone hydrate

Not identified in the human organism

1:3:5(10):7-Oestra-tetraen-3-ol-17-one
Equilin, ♀
 Urine of pregnant mares

1:3:5(10):6:8-Oestra-pentaen-3-ol-17-one
Equilenin, ♀
 Urine of pregnant mares

Not identified in the human organism

Androstan-3-on-17β-ol
Dihydrotestosterone, ♂
 Androstanolone; synthetic

Androstane-3α:17β-diol
Androstanediol, ♂
 Dihydroandrosterone; synthetic

Androstane-3:17-dione
Androstanedione, ♂
 Testes of swine

4-Androsten-3-on-17β-ol
17β-Testosterone, ♂²
 Dehydroandrostan-17-ol-3-one; (17β-form: *trans*-testosterone)

Androstan-3α-ol-17-one
Androsterone, ♂
cis-Androsterone, *epi*androsterone; urine

Androstan-3β-ol-17-one
***epi*Androsterone**, weak ♂
trans-Androsterone, *n*-androsterone, *iso*androsterone; urine

5-Androsten-3β-ol-17-one
Dehydro*epi*androsterone, ♂
 Dehydro*iso*androsterone; urine, metabolite of adrenocortical hormones

4-Androstene-3:17-dione
4-Androstenedione, ♂
 Metabolite of adrenocortical hormones

Androstan-3α-ol-11:17-dione
11-Ketoandrosterone, ♂
 Urine, metabolite of adrenocortical hormones

Androstane-3α:11β-diol-17-one
11-Hydroxyandrosterone, ?
 Urine, metabolite of adrenocortical hormones

9(11)-Androsten-3α-ol-17-one
9(11)-Androstenolone, ♂
 Urine (formed from androstenediolone, a metabolite of adrenocortical hormones, during hydrolysis of urine)

4-Androstene-3:11:17-trione
Adrenosterone, ♂
 Adrenal cortex

Aetian-3α-ol-17-one
α-Aetianolone, ×
 α-Aetiocholanolone; metabolite of testosterone and adrenocortical hormones

Aetian-3α-ol-11:17-dione
11-Ketoaetianolone, ×
 11-Ketoaetiocholanolone; urine, metabolite of adrenocortical hormones

Aetiane-3α:11β-diol-17-one
Aetianediolone, ×
 Aetiocholanolone, hydroxyaetiocholanolone; urine, metabolite of adrenocortical hormones, rare in healthy organism, frequent with malignant tumours

9(11)-Aetien-3α-ol-17-one
9(11)-Aetienolone, ×
 Aetiocholanolone; urine, oxidation product of aetiane-3α:11β-diol-17-one (11-hydroxyaetianolone)

4-Pregnen-21-ol-3:20-dione
Cortexone, ○
 Desoxycorticosterone, 21-hydroxyprogesterone, substance Q (REICHSTEIN)

4-Pregnen-18-al-11β:21-diol-3:20-dione
Aldosterone, ○
 Electro cortin

Not identified in the human organism

4-*iso*Pregnen-20-in-17β-ol-3-one
Anhydrohydroxyprogesterone, ●, ♀, ♂
 Pregneninolone, 17-ethinyl-testosterone; synthetic

5-Pregnen-3β-ol-20-one
Pregnenolone, weak ♂
 Swine

4-Pregnene-17β:20α:21-triol-3-one
Pregnenetriolone, ?
 Synthetic

4-Pregnene-3:20-dione
Progesterone, ●
 Corpus luteum hormone, luteohormone, corporin, progestone, progestin, progesteon

Pregnane-3α:20α-diol
Pregnanediol, ×
 Urine, metabolite of progesterone and adrenocortical hormones

Pregnan-3α-ol
Pregnanol, ×
 Urine

Pregnan-3α-ol-20-one
α-Pregnanolone, ×
*epi*Pregnanolone; urine

Pregnane-3:20-dione
Pregnanedione, ×
 Urine

Pregnan-3α-ol-11:20-dione
11-Ketopregnanolone, ×
 Urine, metabolite of adrenocortical hormones

Adrenocortical hormones

4-Pregnene-11β:17α:21-triol-3:20-dione
Hydrocortisone, ○
 17-Hydroxycorticosterone, compound F (KENDALL), substance M (REICHSTEIN)

4-Pregnene-11β:21-diol-3:20-dione
Corticosterone, ○
 Compound B (KENDALL), substance H (REICHSTEIN)

alloPregnane-3α:20α-diol
α-*allo*Pregnanediol, ×
 Urine, metabolite of progesterone and adrenocortical hormones

alloPregnane-3β:20α-diol
β-*allo*Pregnanediol, ×
 Urine

alloPregnan-3α-ol-20-one
α-*allo*Pregnanolone, ×
 Urine

alloPregnan-3β-ol-20-one
β-*allo*Pregnanolone, ×
 Urine

4-Pregnen-21-ol-3:11:20-trione
11-Dehydrocorticosterone, ○
 Compound A (KENDALL)

4-Pregnene-17α:21-diol-3:11:20-trione
Cortisone, ○
 17-Hydroxy-11-dehydrocorticosterone, compound E (KENDALL), substance Fa (REICHSTEIN), compound F (WINTERSTEINER)

In the chemical formulae :

numbers = carbon atom with a double bond†, or
 = carbon atom to which the substituent group (hydroxyl group, keto-group, etc.) is attached.

di, tri, tetra, penta = 2, 3, 4, 5

al = aldehydo-group

an = saturated bond

en = double bond

ol = hydroxyl group

on = keto-group

desoxy = one O-atom less

anhydro = one H₂O less

dehydro = two H-atoms less

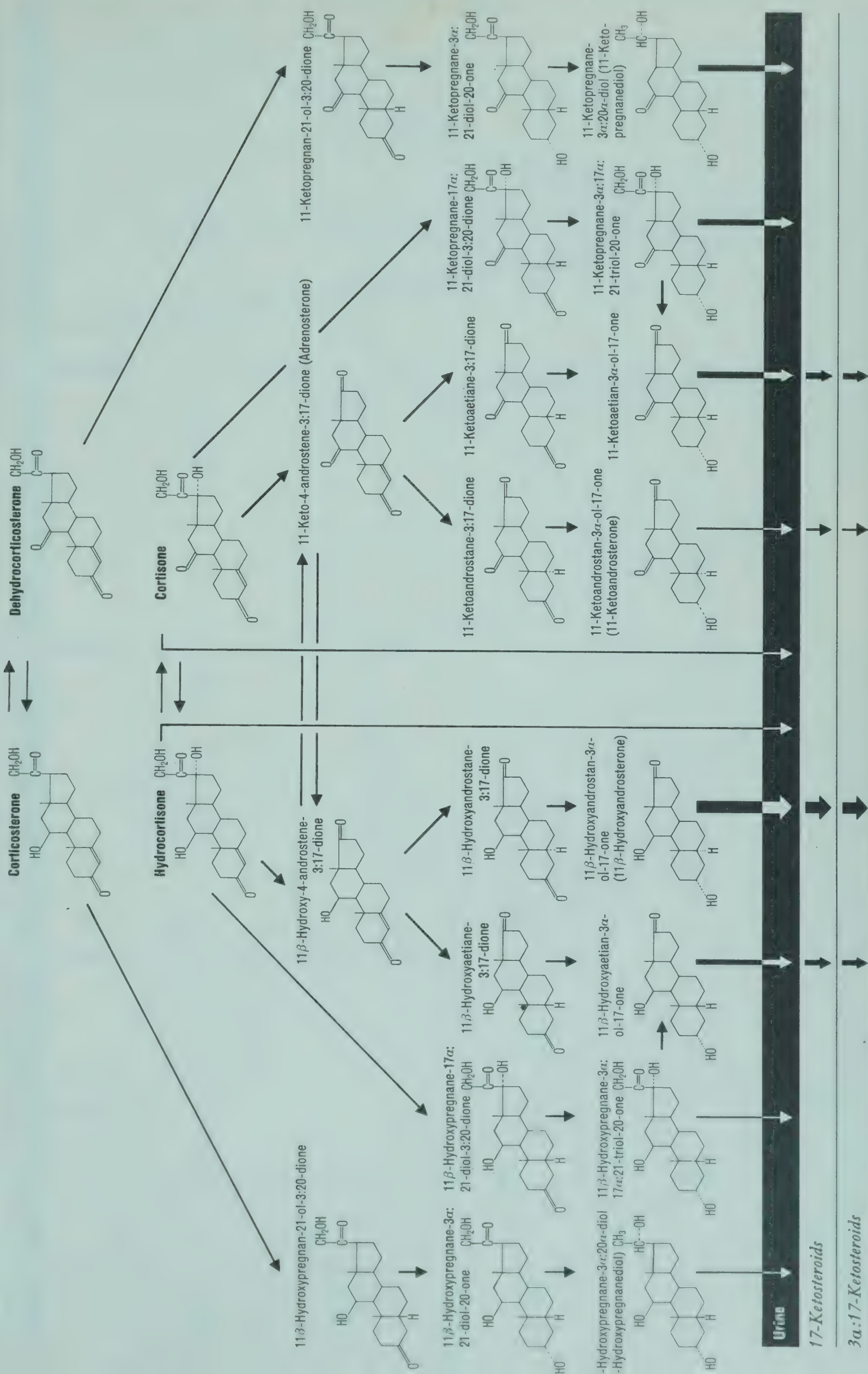
dihydro = two H-atoms more

† Double bonds between carbon atoms having successive numbers (e.g. between C₅ and C₆) are indicated only by the lower number (e.g. 5). Double bonds between carbon atoms with non-successive numbers are indicated by both numbers, the second being in brackets [e.g. between C₈ and C₁₀ = 5(10)].

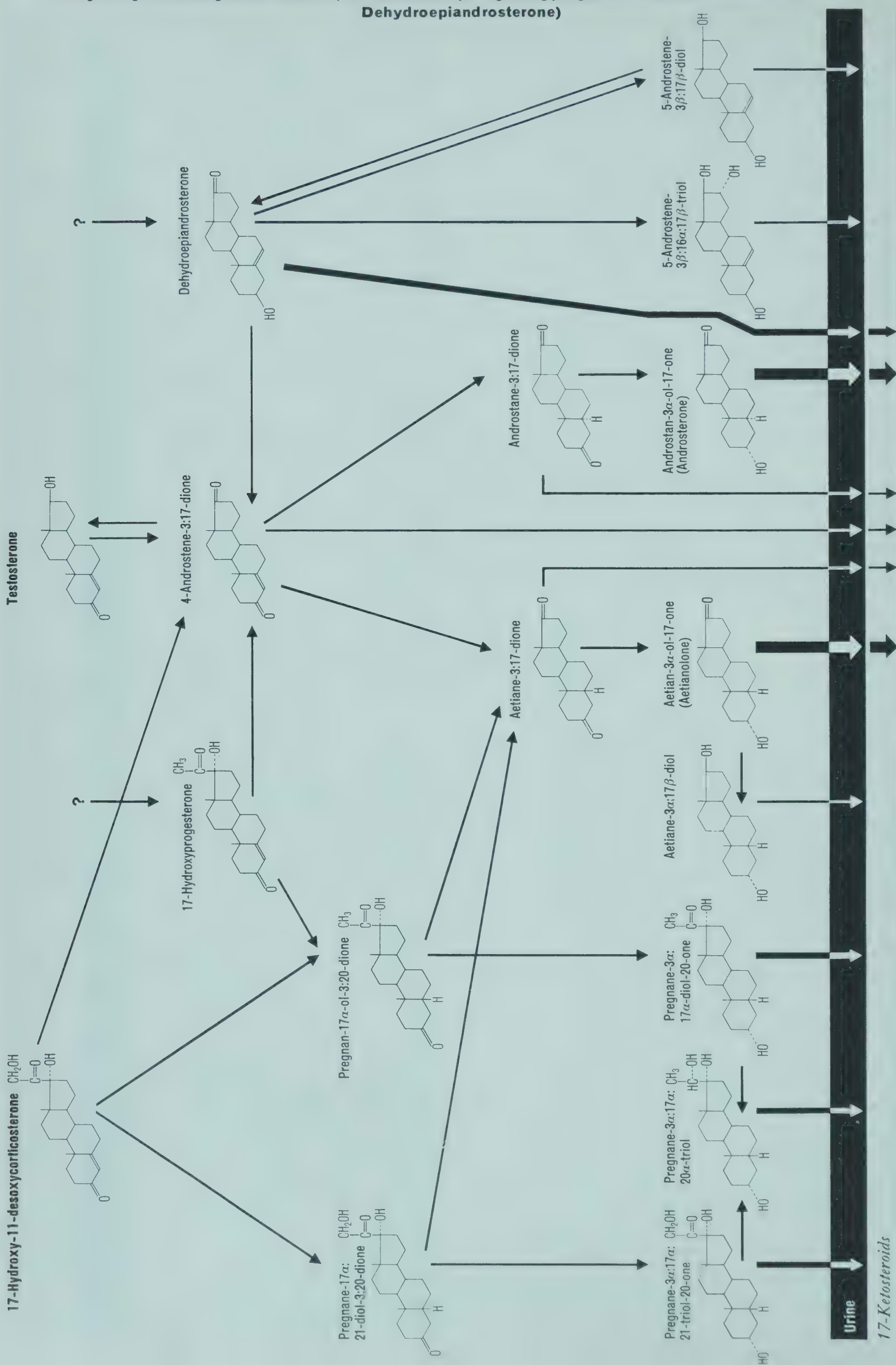
¹ For explanation of the α- and β-configurations see the previous page (*not* valid for the *synonyms* given above, applies only to the designations in **medium face grotesque type**).

² In 1950 it was established that in natural *testosterone* and *oestradiol* the hydroxyl group at C₁₇ was in the β-position instead of the α-position as previously believed. The present 17β-testosterone and 17β-oestradiol therefore correspond to the former α-testosterone and α-oestradiol.

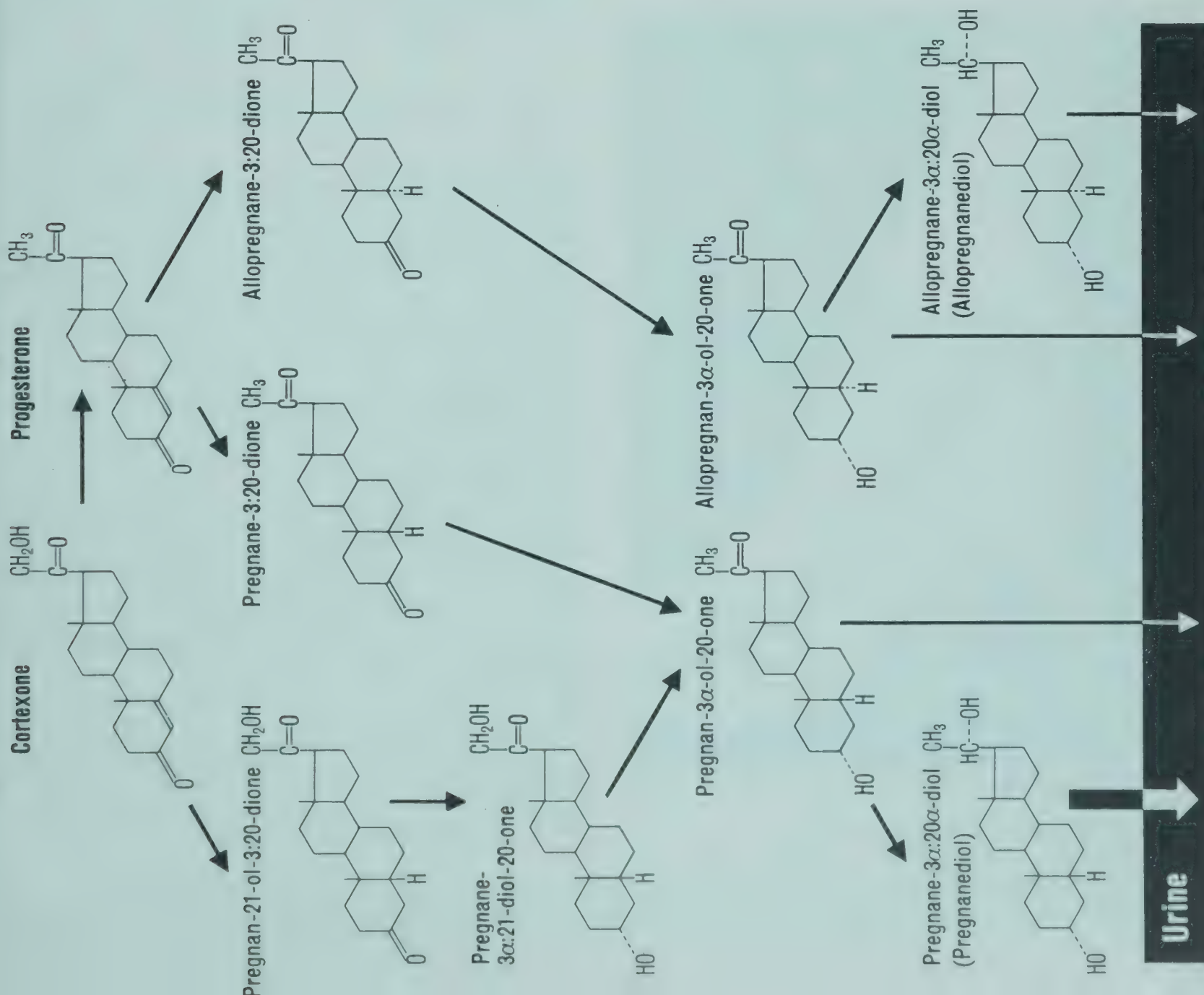
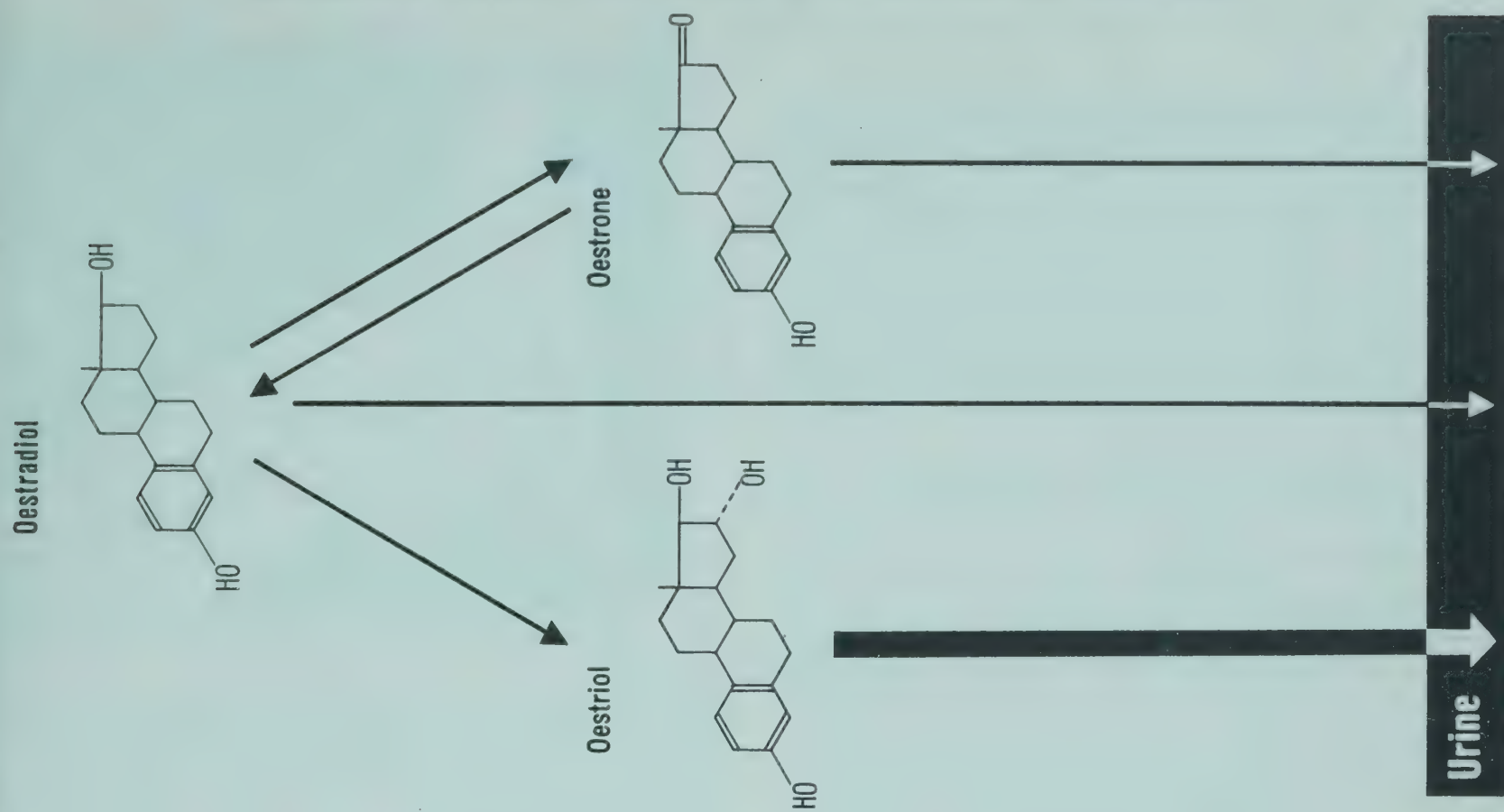
³ According to the rules adopted by the 1950 London conference on the nomenclature of the steroids the trivial name aetianic acid should be used for aetiocholanolic acid. Cf. CAHN et al., *Chemistry and Industry*, Special Issue, 1951.



17-Hydroxy-11-desoxycorticosterone, Testosterone (17-Hydroxyprogesterone, 4-Androstene-3:17-dione, Dehydroepiandrosterone)



Cortexone (Desoxycorticosterone), Progesterone, Oestradiol



17-Ketosteroids

Chemistry

The 17-ketosteroids, so named because of the keto-group at C₁₇, (see diagrams on pages 197 and 198) belong to the C₁₉ group of steroids. They fall into two sub-groups of some clinical significance, the 3 α -hydroxy- and 3 β -hydroxy-17-ketosteroids, known for short as α - and β -17-ketosteroids (see diagrams on pages 197 and 198).

Methods of assay

Total 17-ketosteroids: colorimetrically by the original method of ZIMMERMANN^{1,2} or by the modified method of DREKTER et al.³.

α - and β -Ketosteroids: by the method of HASLAM and KLYNE⁴ or of BUTT et al.⁵.

For chromatographic methods and a general discussion on the assay of ketosteroids, see⁶.

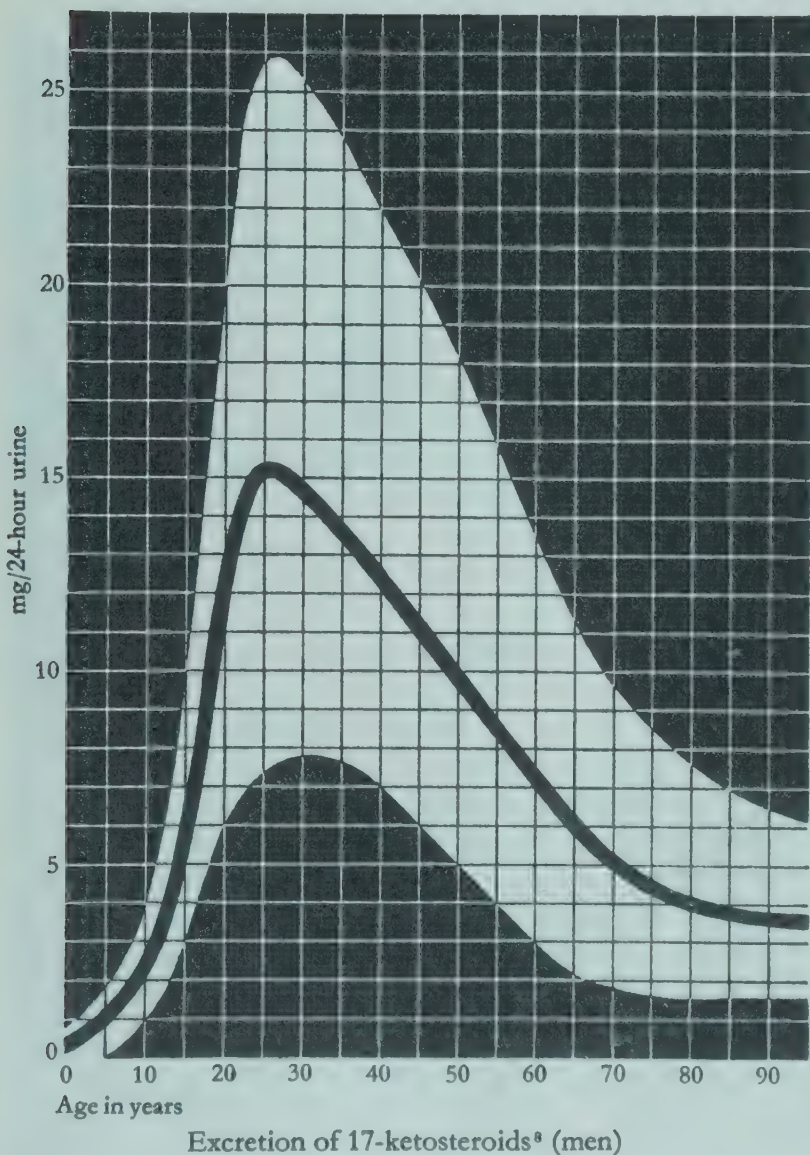
Ketosteroids in 24-hour urine

Total 17-ketosteroids during growth⁷

Age in years	17-Ketosteroids in mg (mean)	Age in years	17-Ketosteroids in mg (mean)
3	0.15	10	1.9
4	0.3	11	2.6
5	0.4	12	3.4
6	0.5	13	4.3
7	0.65	15	6.3
8	0.95	16	7.2
9	1.4	17	8.1

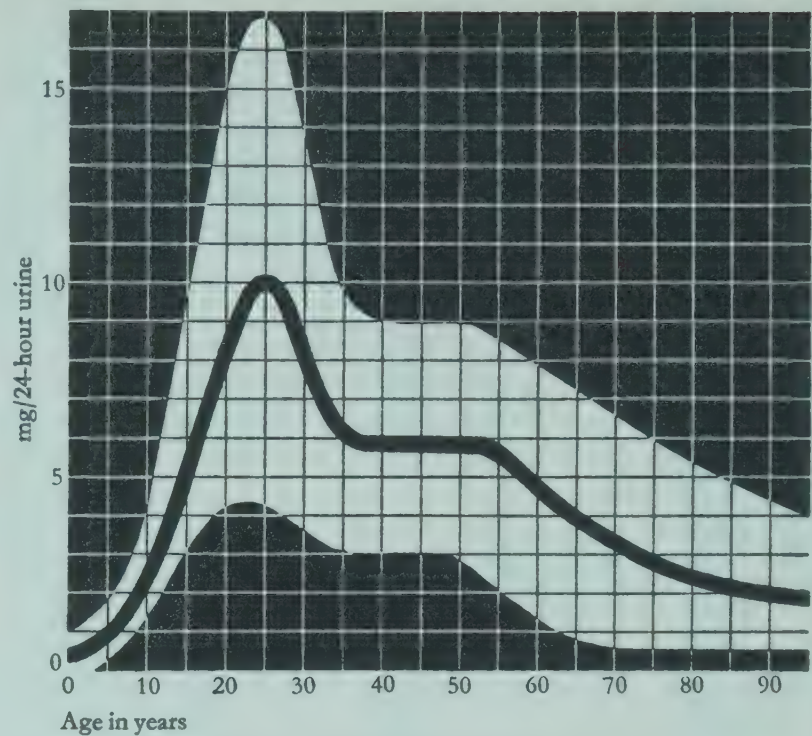
Total 17-ketosteroids in adults

Heavy line: mean values. The white area indicates the zone which includes 97-98% of persons.



Bibliography

¹) ZIMMERMANN, W., *Hoppe-Seyl. Z. physiol. Chem.*, **233**, 257, 1925. ²) ZIMMERMANN, W., *Hoppe-Seyl. Z. physiol. Chem.*, **289**, 91, 1952. ³) DREKTER et al., *J. clin. Endocr.*, **12**, 55, 1952. ⁴) HASLAM and KLYNE, *Lancet*, **1**, 285, 1952. ⁵) BUTT et al., *Biochem. J.*, **42**, 447, 1948. ⁶) *Recent Progr. Hormone Res.*, **9**, 113-245, 1954. ⁷) TALBOT et al., *Amer. J. Dis. Child.*, **65**, 366, 1943. ⁸) HAMBURGER, C., *Acta endocr.*, **1**, 19, 1948. ⁹) RUBIN et al., *Recent Progr. Hormone Res.*, **9**, 213, 1954.



Excretion of 17-ketosteroids⁸ (women)

α -17-Ketosteroids in young adults (19-35 years)⁹

Total α -17-ketosteroids

Men	Women
8.2-15.8; mean 12.0	6.8-14.0; mean 10.4
Standard deviation $\sigma = 1.9$	Standard deviation $\sigma = 1.8$

The α -17-ketosteroid fraction amounts to 80-90% of the total ketosteroids^{4,5}.

The most important components of the α -17-ketosteroids, as also of the total 17-ketosteroids, are⁹

Component	Amount					
	Men			Women		
	Range	Mean	Standard deviation	Range	Mean	Standard deviation
α -Actianolone	2.71-5.07	3.89	0.59	1.93-4.17	3.05	0.56
Androsterone	2.22-4.50	3.36	0.57	2.62-4.89	3.80	0.59
11-Hydroxy-androsterone	0.47-0.99	0.73	0.13	0.52-1.04	0.78	0.13
11-Ketoactianolone	0.43-0.65	0.51	0.07	0.25-0.61	0.49	0.12
11-Hydroxy-aetianolone	0.13-0.57	0.35	0.11	0.15-0.43	0.29	0.07
11-Ketoandrosterone	0.23-0.47	0.35	0.06	0.15-0.27	0.21	0.03

β -17-Ketosteroids

In healthy subjects the β -17-ketosteroids amount to at the most 20% of the total 17-ketosteroids^{4,5}.

Clinical significance

In men at least 50% and in women the whole of the 17-ketosteroids of urine consist of metabolites of the adrenocortical steroids. In men some of the degradation products of testosterone also appear in the 17-ketosteroid fraction. The total quantity of 17-ketosteroids is therefore primarily a measure of the activity of the adrenal cortex (see Corticotropin, pages 182 and 183).

The origin of the most important 17-ketosteroids has been set out in the previous section.

In healthy subjects the β -fraction constitutes at the most 20% of the total 17-ketosteroid fraction^{4,5}. In cases of malignant tumours of the adrenal cortex it is markedly increased (up to 50% of the total fraction) and can therefore be regarded as an important indication in differential diagnosis. In hyperplasia of the adrenal cortex the total fraction is always markedly increased but the ratio of the α - and β -fractions remains normal.

Androgens (for structural formulae see pages 197 and 198, for function see page 204)

The androgens are those steroid hormones which exhibit a typically viriligenic activity in the capon comb growth test.

A number of steroids with androgenic activity are listed below (in order of activity):

1 mg has the same activity as	Androsterone ¹ (mg)
Testosterone	6.7
Androsterone	1.0
4-Androstene-3:17-dione	0.83
Androstane-3:17-dione	0.83–0.77
Dehydroepiandrosterone	0.5
Androstane-3 α :11 β -diol-17-one (11-hydroxyandrosterone)	0.33
Androstane-3 α :17 α -diol	0.28
Adrenosterone	0.2
17-Hydroxyprogesterone	0.2

Testosterone is regarded as the actual hormone of the testes; it can be isolated from animal testes but it has not yet been possible to obtain it from the human organ. It occurs in two stereoisomeric forms, distinguished by the position of the OH-group at C₁₇ in relation to the methyl group at C₁₃. The β -(*cis*)-form has the greater activity. Apart from testosterone, testicular extracts contain a so-called X-factor (LAQUEUR) which markedly increases the activity of testosterone. This factor is very probably not a chemical compound which is per se a promoter of activity. Its effect is possibly explicable by the fact that testosterone occurs in testicular extracts only in the form of esters, for example with fatty acids. These esters are absorbed only slowly, so that the activity of the hormone is significantly increased as a result of the more

constant action (as in exogenous administration at intervals). This marked increase in activity compared with free testosterone is shown, for example, by the synthetic propionic, butyric and valeric esters of testosterone. – For degradation products of testosterone, see page 198 and 17-Ketosteroids (previous page).

The increased urinary excretion of androsterone observed in adrenocortical hyperplasia combined with virilism is simulated by 9(11)-androsten-3 α -ol-17-one². This compound can only be separated with great difficulty from androsterone (preferably by infra-red spectrometry) owing to its very similar chemical properties and is therefore normally included in the “androsterone” fraction. Unlike androsterone, however, it is not a degradation product of testosterone but arises in the hydrolysis of urine from androstene-3 α :11 β -diol-17-one (11-hydroxyandrosterone), a metabolite of hydrocortisone and cortisone (see page 197). In interrenal virilism the androsterone content of the urine is normal.

The daily urinary excretion of androgens, expressed as androsterone, the principal androgen in urine (testosterone is excreted only in traces), amounts to: children (both sexes) up to 10 years, 0.05–0.2 mg; young adult men, 3–10 mg, mean 7 mg; young adult women, 3–10 mg, mean 5 mg (CANTAROW and TRUMPER, *Clinical Biochemistry*, Philadelphia, 1946).

In men⁴ the urinary androgen excretion falls slowly with age, while the oestrogen and corticosteroid excretion remains constant (cause of prostate hypertrophy?). In women⁴ the androgen excretion likewise falls slowly with age, while the oestrogen excretion falls abruptly at the menopause.

Unit. The former international unit of androgenic activity (0.1 mg androsterone) was abolished in 1950. The present biological unit of androgenic activity is the capon unit (C.U.) = the minimal quantity which, administered on two successive days, causes a 20% enlargement of the comb; it corresponds roughly to the activity of 0.1 mg of androsterone.

Methods of test and assay. Biological: on capon comb (see Unit) and cockscomb. For chemical methods see *Recent Progr. Hormone Res.*, 9, 1954.

¹) Calculated from a summary by ABDERHALDEN, R., *Vitamine, Hormone, Fermente*, Basle, 1953, page 155. ²) Oestradiol has also been identified in the testes (GOLDZIEHER and ROBERTS, *J. clin. Endocr.*, 12, 143, 1952). ³) DOBRINER and LIEBERMANN, in GORDON, *Symposium on Steroid Hormones*, Madison, Wisc., 1950. ⁴) KIRK, J. E., *J. Gerontol.*, 6, 253, 1951.

Oestrogens (for structural formulae see page 199, for function see page 204)

Chemistry

All naturally-occurring oestrogenic substances are unsaturated polycyclic alcohols or keto-alcohols. They are easily soluble in ether, alcohol, chloroform, acetone and vegetable oils, insoluble in water. As a result of their phenolic structure they are also easily soluble in aqueous alkalis, permitting their ready separation from androgens in the same urine fraction.

The actual oestrus hormone appears to be the oestradiol formed in the follicles, by far the most actively oestrogenic of all the known female sex hormones. It occurs in an active β - and an inactive α -form (position of the OH-group at C₁₇ with respect to the methyl group at C₁₃—as with testosterone). As in the case of testosterone the esters of oestradiol, particularly the benzoic ester, are more slowly absorbed and thus have a markedly greater hormonal action on the organs concerned than the free compound.

In addition to the relatively small amount of oestradiol, human urine, blood and follicular fluid contain oestrone and oestriol in far larger quantities¹. These have been and still are largely regarded as degradation products of oestradiol. However, more recent studies² of the metabolism of oestrone (and also of progesterone and cortexone) with the aid of ¹⁴C-labelled hormones have thrown doubt on whether they can be regarded wholly as such. The studies showed that after injection of the marked hormones there was a rapid elimination of metabolites through saliva, bile, gastro-intestinal tract and lungs in varying proportions according to individual and species. Fractionation of hydrolyzed urine revealed radioactive ether-soluble neutral compounds, acids, ketonic phenols, alcoholic phenols and simple water-soluble compounds. In particular radioactive urea in urine and radioactive carbonic acid in expired air, which could only have originated from the hormone administered, were found. These observations at least show that the course of metabolic processes is quite other and more complicated than one is led to assume from laboratory experiments and the logical considerations based on them.

Unit

Oestrone: 1 international unit = 0.0001 mg. There is in addition the international unit of oestradiol benzoate: 1 I.B.U. = 0.0001 mg oestradiol benzoate; this is used only for pharmaceutical preparations containing oestradiol benzoate.

The mouse unit (M.U.) and rat unit (R.U.) = minimum amount of oestrogens which causes oestruation (rutting) in castrated female animals.

Methods of test and assay

Chemical-biological methods using castrated mice^{3–6} and rats¹ (here also a review of other methods), chromatographic methods⁷. See also *Recent Progr. Hormone Res.*, 9, 1954.

Activity of individual oestrogens

1 milligram oestriol	corresponds to	75 mouse units
1 » oestrone	» »	8000 » »
1 » oestradiol	» »	75,000 » »

Oestrogens in blood and urine

Men : urinary oestrogen value fairly constant.

Women : urinary and serum oestrogen values rise and fall together according to the stage of the menstrual cycle or pregnancy (maximum at the time of ovulation or towards the end of pregnancy).

Children : see figure 2 on the following page.

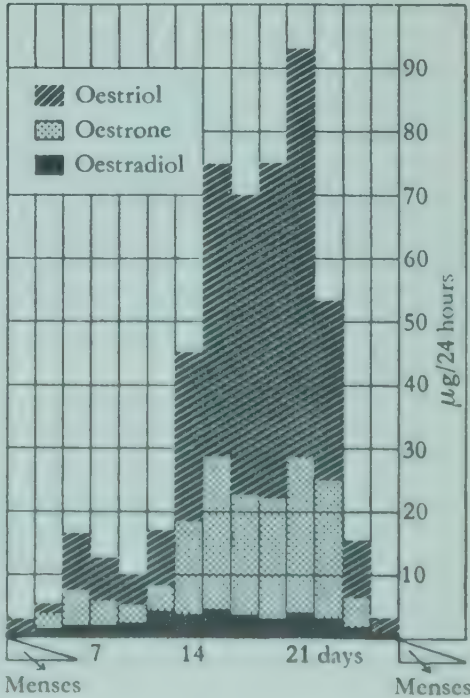
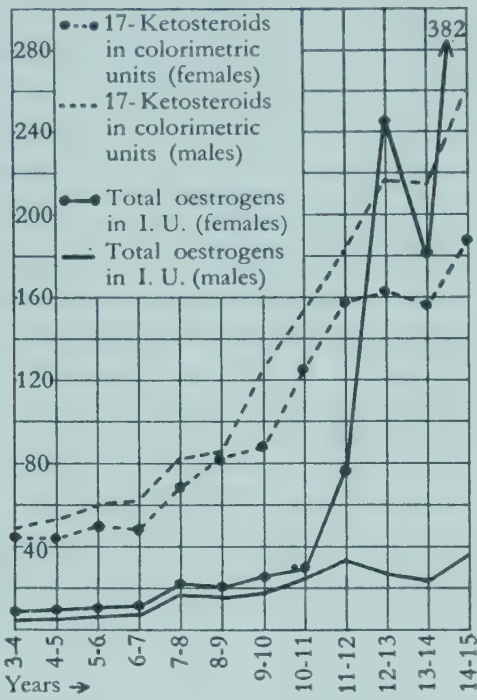


Fig. 1. Total and individual oestrogen values in 24-hour urine during the course of the menstrual cycle. After SMITH and SMITH¹.

Oestrogens (concluded)

Fig. 2. 17-Ketosteroids and oestrogens in 24-hour urine of children and adolescents (averages of numerous determinations). After NATHANSON et al.⁸.



Total oestrogens in serum and urine (men and women) after RAKOFF et al.⁹

Oestrogens in	Women					Men
	Day of menstrual cycle				Meno- pause	
	7	14	21	28		
24-hour urine (in I.U.)	65-160	160-660	160-660	30-110	10-65	25-100
Mean	110	330	500	65	below 65	50
Serum (in M.U.) ¹⁰	trace - 6	3-9	3-9	0-3	0 - trace	-

¹⁾ Cf. SMITH and SMITH, *Recent Progr. Hormone Res.*, **7**, 209, 1952. ²⁾ HEARD, H. D. R., *ibid.* (Discussion), **7**, 253, 1952. ³⁾ FRANK and GOLDBERGER, *Proc. Soc. exp. Biol.*, **27**, 73, 1929. ⁴⁾ FRANK and GOLDBERGER, *ibid.*, **32**, 1663, 1935. ⁵⁾ FRANK, R. T., *J. Amer. med. Ass.*, **97**, 1852, 1931. ⁶⁾ FRANK et al., *Proc. Soc. exp. Biol.*, **38**, 853, 1938. ⁷⁾ BUSH, I. E., *Biochem. J.*, **50**, 370, 1952. ⁸⁾ NATHANSON et al., *Endocrinology*, **28**, 851, 1941. ⁹⁾ RAKOFF et al., *Clinical Biochemistry*, Philadelphia, 1945. ¹⁰⁾ FLUHMAN, C. F., *Endocrinology*, **18**, 705, 1934. ¹¹⁾ SMITH et al., *Amer. J. Obstet. Gynec.*, **45**, 15, 1943. ¹²⁾ SMITH and SMITH, *Amer. J. Physiol.*, **39**, 405, 1940.

Individual oestrogens in 24-hour urine (women), after SMITH et al.¹¹

Day of menstrual cycle	Total oestrogens I.U.	% Oestradiol	% Oestrone	% Oestriol
1- 3	100	67	0	33
7- 8	215	49	18	33
14-15	530	30	20	50
20-21	615	34	23	43
26-28	100	45	20	35

Pregnancy: During pregnancy the placenta produces oestrogens in large quantities. Cf. page 204.

Pregnancy: Oestrogens in serum (after RAKOFF et al.⁹)

Weeks since last menstruation	Serum oestrogens in I.U./100 ml	
	Range	Mean
2	15- 80	30
4	15- 100	40
8	30- 125	60
12	45- 165	80
16	80- 200	125
20	165- 250	165
24	165- 330	250
28	200- 400	330
32	250- 600	400
36	330- 750	500
40	330-1500	600

Pregnancy: Oestrogens in 24-hour urine (after SMITH and SMITH¹²)

Weeks since last menstruation	24-hour urine					
	Oestradiol R. U. mg		Oestrone R. U. mg		Oestriol R. U. mg	
12	450	0.0225	50	0.033	1000	0.5
16	1000	0.05	250	0.166	4000	2.0
21	1330	0.066	670	0.445	8000	4.0
25½	2000	0.10	700	0.465	15,000	7.5
27	1330	0.066	400	0.267	20,000	10.0
29	1330	0.066	1330	0.89	20,000	10.0
31	1200	0.06	400	0.267	20,000	10.0
33	1500	0.075	1000	0.667	22,500	11.1
35	1000	0.05	330	0.22	25,000	12.5
37	1000	0.05	1000	0.667	53,000	26.5
39	1330	0.066	670	0.45	60,000	30.0
39½	400	0.02	0	-	20,000	10.0

Progesterone (for structural formula see page 199, for function see page 204)

Progesterone, the hormone of the corpus luteum, is very closely allied to the adrenocortical hormones. It occurs in two distinct crystalline forms, the α - and β -forms.

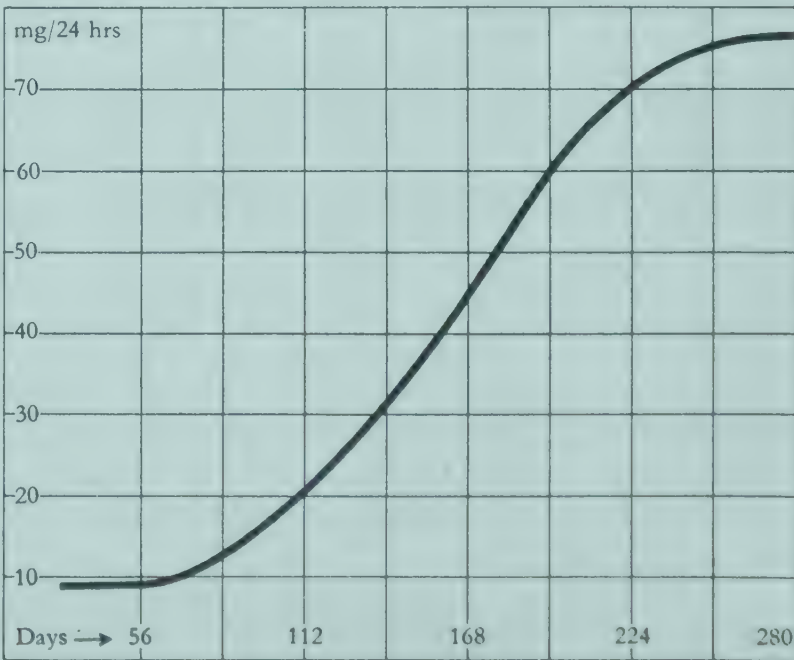
In urine progesterone emerges mainly as the glucuronic esters of its degradation products pregnane-3 α :20 α -diol and allopregnane-3 α :20 α -diol, present methods of assay determining these two compounds together as "pregnanediol", although the latter name applies strictly only to pregnane-3 α :20 α -diol¹ (see page 199). For the sake of simplicity, however, the expression "pregnanediol" will be used in the following text to indicate the mixture of these two compounds. The pregnanediol of urine is not only a degradation product of progesterone but also of cortexone (desoxycorticosterone) but since the latter is present in the organism only in very small quantities its contribution to the excretion of pregnanediol may be ignored. If cortexone is administered exogenously, however, the excretion of pregnanediol is considerably increased, in proportion to the dosage, and this fact should not be overlooked when the pregnanediol value is used as a test for pregnancy.

A method of assay very suitable for routine clinical purposes, and more reliable than that of GUTERMAN^{2, 3}, is the method of SOMMERVILLE, MARRIAN and KELLAR¹.

In the normal menstrual cycle the excretion of pregnanediol in urine commences immediately after ovulation with ca. 2-5 mg per day, rising to 5-10 mg. Several days before menstruation commences the value falls below 5 mg and finally, 24-28 hours after the start of menstruation, to zero. The total quantity excreted during the menstrual cycle amounts to (20)40-50(80) mg (SUNDERMAN and BOERNER, *Normal Values in Clinical Medicine*, Philadelphia, 1950).

The urine values during pregnancy are from VENNING, E.H., *J. biol. Chem.*, **126**, 595, 1938:

Excretion of pregnanediol during pregnancy (24-hour urine)



Progesterone (concluded)

Weeks since last menstruation	mg in 24-hour urine range	mean
2	2– 10	6
4	5– 15	10
8	5– 15	10
12	8– 20	12
16	8– 30	20
20	16– 32	25
24	20– 60	40
28	35– 80	50
32	40– 80	60
36	50–100	68
40	50–120	70

Some authors have reported a fall in the value 1–2 weeks before the birth but this is not a regular feature.

Unit. International unit = 1 milligram progesterone.
Rabbit unit = ca. 0.6 mg.

Methods of test and assay.
See SOMMERVILLE, MARRIAN and KELLAR¹.

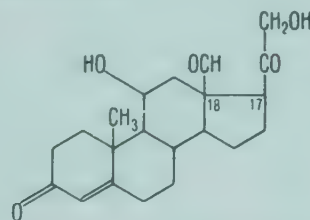
¹) SOMMERVILLE et al., *Lancet*, 2, 89, 1948. ²) GUTERMAN, H. S., *J. clin. Endocr.*, 4, 262, 1944. ³) GUTERMAN, H. S., *ibid.*, 5, 407, 1945.

Adrenocortical hormones (cf. Corticotropin, pages 182–189; for structural formulae, see pages 197–199)

The adrenocortical hormones belong to the C₂₁ group of hormones and are thus chemically closely allied to the other steroid hormones. This fact is reflected in the biological relationship in that in the absence of the cortex the sex hormones have a distinct life-prolonging effect. It is also evidenced by the fact that certain adrenocortical substances and metabolites of adrenocortical hormones exhibit androgenic, progestational and oestrogenic activity. Adrenocortical dysfunction, e.g. through hyperplasia or neoplasm, can therefore lead to interrenal virilism in women or to interrenal feminism (rare) or pubertas praecox in men: cf. 9(11)-androstenolone and androsterone (Androgens, page 201).

More than 25 different steroids have so far been isolated from the adrenal cortex. Six of these show a substitutive effect in the survival test on adrenalectomized animals and are therefore now recognized as adrenocortical hormones: hydrocortisone (17-hydroxycorticosterone), cortisone, corticosterone, 11-dehydrocorticosterone, 17-hydroxy-11-desoxycorticosterone and cortexone (desoxycorticosterone). Apart from the known steroids, however, the cortex contains other unknown substances (in the so-called amorphous fraction) which also have a distinct life-prolonging effect.

Recently a steroid with extraordinarily strong effect on mineral metabolism has been isolated from this fraction (1953, SIMPSON, TAIT, WETTSTEIN, NEHER, v. EUW, and REICHSTEIN)¹. This adrenocortical hormone, named **aldosterone** on account of its aldehydo-group at C₁₈ (see structural formula)², induces in rats a 25 times stronger sodium retention and a 5 times stronger potassium retention than cortexone³, while in contrast to the latter it has hardly any effect on water elimination. The first clinical tests⁴ showed that administration of minimal quantities (2.5–3.3 µg/day/kg body weight) brought about the disappearance of the clinical ADDISON symptoms. Aldosterone also has an effect on carbohydrate metabolism, while in the small amounts administered it has no effect on nitrogen metabolism. It is still too early to assess the significance of this substance in relation to the other adrenocortical hormones but it is at least evident that it differs from them not only in respect of structure and therefore mode of biosynthesis but also in its relatively high potency and low concentration in biological fluids (cf. oestrogens), and in the manner in which its secretion is controlled. There is evidence that the latter is not subject to ACTH stimulation⁵. The synthesis of aldosterone has recently been reported by WETTSTEIN et al., the product possessing biological activity identical with the natural hormone.



Structural formula of aldosterone²

Approximate comparative activities of adrenocortical hormones⁶

Hormone	Survival (rats)	Renal function (dogs)	Electrolyte metabolism (dogs)	Muscular work (rats)	Liver glycogen (rats)	Diabetogenic effect (rats)
Corticosterone	1–2	2	1–2	3	3	3–4
11-Dehydrocorticosterone.	1–2	2	1–2	2	2	3–4
Cortisone	2	1	?	4	4	5
Hydrocortisone	2	1	?	4	4	5
Cortexone	4	4	5	1	1	1
Amorphous fraction	+ 5	+ 5	?	1–2	1	?

In this connection it should be emphasized that there are marked differences in the reactions of different species to the various adrenocortical hormones, particularly between rats and man.

As a result of the earlier availability of certain adrenocortical hormones, e.g. cortexone, and ignorance of the differences in the reactions of different animal species, the progress of research in the field of these hormones led at one time to some of them being overrated. Today the improved availability of all the known adrenocortical hormones together with improvements and refinements in the methods of investigation and assay permit a better assessment of the significance of the individual hormones. It is now certain that the hormone the most abundantly secreted by the corticotropin-stimulated cortex is hydrocortisone, followed by corticosterone, while all the other steroids are present in the blood only in very small amounts. It should not be overlooked, however, that the steroids secreted in relatively small quantities, among which are numerous substances with unknown activity, may in certain circumstances play important roles. In any case, however, the functions of these secondary steroids are so overshadowed by the effects of hydrocortisone that the latter may without sensible error be identified with the corticotropin and stress effects.

In the literature a distinction between *mineralo-* and *gluco-*corticosteroids is often found. Since there are only quantitative differences in the overlapping activities of the individual hormones, this question has intentionally been dealt with in the section “Corticotropin” (pages 182–189) where the biological aspects of the corticosteroids are also dealt with. All the adrenocortical hormones have an effect both on mineral and on organic metabolism and a distinction between mineralo- and gluco-corticosteroids could only be appropriate to a comparison of the two extremes cortexone and cortisone. Corticosterone, for example, shows both effects to the same degree, and hydrocortisone possesses in addition to its strong effect on carbohydrate metabolism a marked electrolyte effect.

A clearer distinction between the corticosteroids may be made on the basis of their chemical structures, where a certain parallelism with their metabolic activities is apparent. The following grouping emerges:

11-O-Corticosteroids, i.e. those with an oxygen atom at C₁₁ – hydrocortisone, corticosterone, 11-dehydrocorticosterone, cortisone (also aldosterone) in contrast to cortexone and 17-hydroxy-11-desoxycorticosterone which have no oxygen atom at C₁₁, and

11-17-O-Corticosteroids, i.e. those with oxygen atoms both at C₁₁ and C₁₇ – hydrocortisone and cortisone

in contrast to corticosterone, cortexone, 17-hydroxy-11-desoxycorticosterone (and aldosterone).

In comparison with cortexone the 11-O-corticosteroids have a stronger effect on carbohydrate metabolism (and usually also on the total organic metabolism); the 11-17-O-corticosteroids show this effect most markedly.

On the degradation of the corticosteroids, see pages 197–199. Over 60 different steroids have up to now been isolated from urine; the majority of these must be metabolites of adrenocortical substances, since they are present also after castration. The majority of the metabolites of the corticosteroids usually appear in the 17-ketosteroid fraction. Cf. Corticotropin, page 182, and 17-Ketosteroids, page 200.

Unit
None; by weight.

Methods of test and assay
11-17-O-corticosteroids in urine, see Corticotropin, page 182.

¹) SIMPSON et al., *Experientia*, 9, 333, 1953. ²) SIMPSON et al., *Experientia*, 10, 132, 1954. ³) DESAULLES et al., *Schweiz. med. Wschr.*, 83, 1088, 1953. ⁴) MACH et al., *Schweiz. med. Wschr.*, 84, 407, 1954. ⁵) SIMPSON, S. A., and TAIT, J. F., *Recent Progr. Hormone Res.*, 11, 183, 1955. ⁶) INGLE, D. J., in GORDON, *Symposium on Steroid Hormones*, Madison, Wisc., 1950, page 150.

Functions of the sex hormones

From the close similarity in the chemical structure of the three principal hormones (testosterone, oestradiol, progesterone) it is highly probable that their chemical relationship is of biological and phylogenetic origin. Hormones of these three types occur in both sexes and are found throughout the vertebrates: they are specific neither for sex nor species. Experimentally the direction and intensity of the hormonal effect is a question of dosage, of the proportions in which they are mixed, of the stage of the menstrual cycle and of the organ on which they act. Although the extent to which absence of the sex hormones affects the development of the sex organs is the greater, the earlier the stage of foetal development, it is quite certain that these hormones have no effect on sex differentiation. Recent studies have shown that the development of female sexual characteristics is inherent in both sexes, i.e. that the development is automatically in the female direction unless it is diverted in the male direction by the testes anlage. The effect of the latter is not, however, exercised through the male sex hormone, since after removal of the testes anlage the development of female characteristics cannot be hindered by administering male sex hormone. It appears rather to be an inductive effect of unknown nature exercised by the testes anlage on the surrounding primitive tissues (transplantation of a testes anlage on to an embryo is likewise followed by female development)¹.

In addition to its sexual activity testosterone shows a marked anabolic action (protein forming, with concomitant effect on energy metabolism)², and may therefore be used therapeutically for the normalization of nitrogen balance disturbed by corticotropin or adrenocortical hormone therapy (see Corticotropin, page 187).

In both sexes the adrenal cortex plays an important role in the production of sex hormones, presumably by providing the precursors.

The individual hormone types, particularly the oestrogens and progesterone, act either antagonistically or synergistically according to the stage of the menstrual cycle and the organ affected. Each of these hormones requires, however, in the phase in which it predominates, the co-operation of the opposite hormone in order that the organs affected may remain capable of functioning biologically (see table below). In this connection see also COURRIER, R., *Interactions between Estrogens and Progesterone*³. The effectiveness is greatly increased by the presence of traces of the opposite hormone: threatened abortion (operative removal of the ovaries) at the commencement of pregnancy can for example be held off with the aid of much smaller doses of progesterone if a little oestradiol is added to it. A similar remarkable co-operation exists between androgens and oestrogens: provided that sufficient follicular hormone is present, androgens have a libido-increasing effect on women, whereas they are otherwise typical female antagonists.

In addition to gonadotropic hormones (pages 179 and 180) the developing placenta produces during pregnancy increasing quantities of progesterone and oestrogens, rapidly surpassing the ovaries in this respect. In the absence of the ovarian and pituitary hormone production that of the placenta suffices to hinder an abortion. This defensive mechanism of the human embryo in late pregnancy is exceptional among mammals (otherwise observed only in the horse and guinea-pig).

Male organism		Androgens	Oestrogens	Progesterone
Development of primary sex organs	General, above all testes, prostate, penis:	+++	antagonist	
	Musculature and connective tissue of access. glands:	?	+	
Development of secondary sexual characteristics		+++++	antagonist	
Psychic behaviour: libido, masculine activity		+++++	antagonist	
Female organism				
Development of primary sex organs	General, above all uterus and ovaries:	partial antag.	+++	0
	Organs of the orgasm:	+	+++	0
Development of secondary sexual characteristics		antagonist	+++++	?
Psychic behaviour: female passivity	antagonist	+++++	+
	libido	+++	+	partial antagonist
Menstrual cycle				
Maturation of ovum		?	+++	+
Proliferation phase		?	+++++	+
Secretion phase		?	+	+++++
Migration of ovum, nidation		?	++	+++
Pregnancy		Always present in large quantities, not subject to cyclic variation		
Inhibition of maturation of further follicles, quiescence of the uterus, relaxation of the uterine muscles (2). Lowering of the Na/K ratio in blood, lowering of the sympathetic tonus (4)			{ antagonist to (2), synergist to (4)	{ +++++
Indispensable for maintenance of pregnancy			++	++
Relaxation of the pelvic girdle, increase of tonus of uterine musculature towards end of pregnancy (2)			+++	anatagonist to (2)
Growth of mammary tissue			++	++
Inhibition of lactation until birth			++	+
Post partum				
Maintenance of lactation		?	++*	++*
Inhibition of lactation at high therapeutic dosage		++ ⁽⁵⁾	+++++	0
Involution of the uterus and preparation for fresh menstrual cycle		?	+++	0

Therapeutic applications. In hypo-, dys- or hyper-function, see table above. The mixture proportions which are optimal for man are unfortunately not yet known. Clinical research on this problem would be worthwhile, particularly in cases of habitual abortion³.

Increase of libido in the paradoxical treatment of mammary carcinoma can often be observed^{4, 5}.

Androgens in very high doses are indicated in cases of advanced mammary carcinoma with diffuse bone metastases in patients before the menopause; after the menopause, particularly with patients over 60, oestrogens are preferable in cases of scirrhus and metastases of similar carcinoma types⁶.

Oestrogens: inoperable prostate carcinoma, peripheral circulatory disturbances, badly healing bone fractures, gastric and duodenal ulcers.

Androgens: Inoperable mammary carcinoma, normalization of negative metabolic balances during corticotropin or adrenocortical hormone therapy, frigidity in women, certain cases of glandular-cystic hyperplasia of the endometrium, endometriosis, dysmenorrhoea, hypertrophy of the prostate.

* Together with the lactogenic and other hormones (see page 180).

¹) MOORE, R. C., in GORDON, *Symposium on Steroid Hormones*, Madison, Wisc., 1950, p. 393. ²) KOCHAKIAN, C. D., *ibid.*, 1950, p. 113. ³) COURRIER, R., *J. Amer. and Horm.*, **8**, 179, 1950. ⁴) BLEULER and ZÜBLIN, *Wien. med. Wschr.*, **100**, 229, 1950. ⁵) RIES, H., *ibid.*, **101**, 278, 1951. ⁶) D'ARGENT et al., *Presse méd.*, **57**, 260, 1949.

Chemistry

Noradrenaline and adrenaline are amino-derivatives of catechol and have very similar properties, rendering them very difficult to separate. Both are sparingly soluble in water but readily soluble in most organic solvents and in aqueous alkalis and acids. Their salts are readily soluble in water.

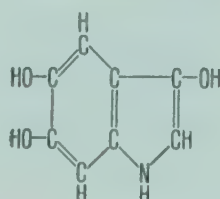
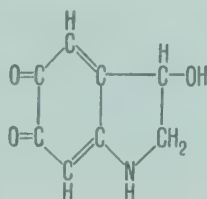
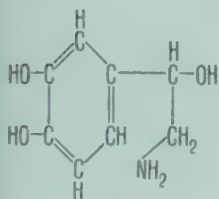
Naturally-occurring noradrenaline and adrenaline are laevo-rotatory. Synthesis yields the racemates, which are only 3–4% as active as the laevo-rotatory forms. Both compounds are extremely easily oxidized to noradrenochrome and adrenochrome respectively. In acid solutions adrenaline oxidizes more rapidly: for example with 0.1-N iodine solution at pH 4 adrenaline is almost completely oxidized, noradrenaline only ca. 10%¹; at pH 6 both are completely oxidized. The difference in the rate of oxidation is used for the separation of the two compounds in solution.

Noradrenaline, $C_8H_{11}O_3N$

Mol. wt. 169.18

Noradrenochrome

Noradrenolutine

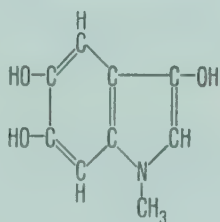
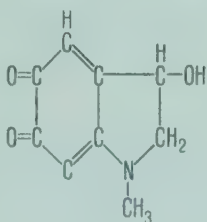
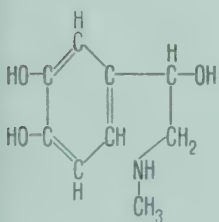


Adrenaline, $C_9H_{13}O_3N$

Mol. wt. 183.20

Adrenochrome

Adrenolutine



Unit

None; by weight.

Methods of test and assay

The following methods are suitable for the determination of noradrenaline + adrenaline or of either compound alone:

1. Biologically: after isolation (by precipitation with aluminium hydroxide², etc.) by the blood pressure of the chloralized, cocaine-sensitized cat³ (sensitivity 0.2 μ g noradrenaline), or on the surviving rat uterus⁴ (sensitivity $1/1000$ μ g adrenaline, for noradrenaline 75–300 times less sensitive).

2. Chemically: a) colorimetrically¹ (sensitivity 10 μ g noradrenaline or adrenaline); b) chromatographically⁵ (sensitivity 2 μ g noradrenaline or adrenaline); c) fluorometrically: adrenaline^{6,7}, noradrenaline and adrenaline⁸ (sensitivity $1/100$ μ g for both). In the latter method the noradrenaline or adrenaline is first adsorbed on alumina, oxidized, and the resultant noradrenochrome or adrenochrome then converted into the fluorescent noradrenolutine or adrenolutine.

Noradrenaline and adrenaline in blood and urine. The blood noradrenaline content amounts to ca. 1–2 μ g, the adrenaline content to some hundredths of this quantity. The 24-hour urine contains ca. 15–45 μ g noradrenaline-equivalent of which ca. 15% is adrenaline^{9–12}. The noradrenaline and adrenaline in urine originates mainly from the central nervous system, since in complete destruction of the adrenals the values remain normal or can even increase¹³. After intravenous infusion of noradrenaline only about 2% of it appears in the urine¹³.

Noradrenaline and adrenaline in the tissues. Noradrenaline¹¹ is found everywhere in the central nervous system in concentrations of ca. 1–2 mg/100 g tissue, the highest concentration being in the thoracic and lumbar ganglia (3–10 mg/100 g), but also in the spleen (0.3–0.4 mg/100 g), the heart, bone marrow and placenta. The adrenaline content of these tissues amounts only to a few per cent of the noradrenaline content.

In the adrenal medulla this ratio is reversed. Here the proportion of adrenaline in the catecholamine fraction (total ca. 7–9 mg per medulla) is 80%, that of noradrenaline hardly 20% (in man; the proportions vary greatly from species to species, the medulla of the rabbit for example contains little or no noradrenaline)^{10,13}. The content of adrenaline is proportional to that of ascorbic acid, the function of which is to protect the secreted adrenaline from oxidation¹⁴.

Physiology and function

Significance of noradrenaline and adrenaline. In view of its concentration in the various tissues and the identity of its effect with excitation of the sympathicus, noradrenaline (or its mixture with a small percentage of adrenaline) is regarded as the natural transmitter of impulses over the central nervous system.

The identification of noradrenaline as the natural sympathomimetic has created considerable uncertainty as to the function of adrenaline, regarded since its discovery as quite certain, and of the adrenal medulla. It is at least certain that the secretion of the medulla does not accentuate the sympathetic tonus, since adrenaline, as will be seen, is a partial antagonist of noradrenaline. The significance of the increased medullar secretion in "emergency" appears in the light of present conceptions of the corticotropin/adrenocortical hormone function to lie in an indirect stimulation of the corticotropin secretion of the pituitary, and thereby of the hormonal secretion of the cortex, through an increase in cell metabolism. This auxiliary effect of adrenaline is not, however, absolutely necessary either for the initiation or for the maintenance of the defensive stress reaction (cf. Corticotropin, section 8, p.184).

Adrenaline as well as noradrenaline is blocked by antiadrenergics (ergotamine, tetraethylammonium chloride, dibenamine).

Influence on blood circulation. In continuous intravenous infusion (0.1–0.3 μ g per minute per kg body weight) the following effects are observed in man (*inter alia* by catheterization of the right heart, FICK principle)^{15,20}: **Noradrenaline:** prompt increase of the mean blood pressure owing to increase of the systolic and diastolic pressure, caused by increase of the peripheral resistance (vasoconstriction). Cardiac performance unchanged or slightly lowered. Owing to the absence of subjective symptoms of any kind the subject usually remains ignorant of the circulatory changes. **Adrenaline:** increase of the mean blood pressure through overcompensation of the constant observable fall in peripheral circulation (vasodilatation) by the corresponding increase in beat frequency and volume. Unpleasant subjective symptoms: tachycardia, palpitations, psychic symptoms.

Noradrenaline and adrenaline thus both cause an increase in blood pressure, but in different ways. With noradrenaline, vasoconstriction, reduced blood supply to all organs, increase of the peripheral resistance, no change in cardiac performance; with adrenaline, increase of cardiac performance, vasodilatation, increased blood supply to all organs, lowering of the peripheral resistance^{16–18, 20, 26}.

With intravenous doses larger than 0.3 µg/min/kg, adrenaline, like noradrenaline, causes vasoconstriction. This occurs pathologically only in hyperactivity of the medulla²¹, e.g. in phaeochromocytoma. The circulatory effects of adrenaline and noradrenaline (up to 0.3 µg/min/kg i.v.) are mutually compensatory.

Influence on the kidneys. Noradrenaline and adrenaline cause a marked reduction in the renal blood circulation, the renal plasma circulation and the glomerular filtration rate²⁵.

Metabolic effects. The metabolic changes caused by adrenaline (increase of B.M.R.²⁴, hyperglycaemia) are absent or significantly smaller with noradrenaline^{15,21}.

Influence on the central nervous system. The symptoms such as restlessness, oppression and anxiety caused by adrenaline are absent with noradrenaline.

Influence on the adrenal cortex. Neither adrenaline nor noradrenaline has any direct action. Indirectly only adrenaline has any effect (increased adrenocortical hormone secretion and the stress reactions thereby made possible, e.g. eosinopenia).

Therapeutic application. Noradrenaline as sympathomimetic without secondary effects. Adrenaline in surgical operations: acute failure of the peripheral circulation and heart; as vasoconstrictive auxiliary in local anaesthesia.

Comparative effects of adrenaline i.v. (0.1–0.3 µg/min/kg) and noradrenaline i.v. (0.1–0.325 µg/min/kg)^{12,15,21–23}.

+ or – = nature and degree of effect; with square surround □ = no significant effect.

	Noradrenaline	Adrenaline
Pulse frequency	—	+
Cardiac performance	□—	+++
Systolic blood pressure	+++	+++
Diastolic blood pressure	++	□+
Total peripheral circulation resistance	+++	—
B.M.R.	□+	++
Blood sugar	□+	+++
Influence on central nervous system .	□	+
Eosinopenia	□	+

The medullar secretion always shows the constant ratio of ca. 20% noradrenaline to ca. 80% adrenaline. The effects of an increased medullar secretion are therefore practically speaking those of adrenaline.

¹) VON EULER and HAMBERG, *Acta physiol. scand.*, **19**, 74, 1949. ²) SHAW, F. H., *Biochem. J.*, **32**, 19, 1938. ³) VON EULER and LUFT, *Acta endocr.*, **3**, 323, 1949, ⁴) GADDUM, J. H., *Methods in Medical Research*, Vol. 3, Chicago, 1950, p. 116. ⁵) GOLDENBERG, M., *Science*, **109**, 534, 1949. ⁶) LUND, A., *Acta pharmacol.*, **5**, 121, 1949. ⁷) LUND, A., *ibid.*, **5**, 231, 1949. ⁸) LUND, A., *ibid.*, **6**, 137, 1950. ⁹) HOLTZ et al., *Arch. exp. Path. Pharmacol.*, **204**, 228, 1947. ¹⁰) VON EULER, U. S., *Ergebn. Physiol.*, **46**, 261, 1950. ¹¹) VON EULER, U. S., *Brit. med. J.*, **1**, 105, 1951. ¹²) GOLDENBERG, M., *Amer. J. Med.*, **10**, 627, 1951. ¹³) HOLTZ and SCHUH-MANN, *Arch. exp. Path. Pharmacol.*, **210**, 1, 1950. ¹⁴) HEARD and WELCH, *Biochem. J.*, **29**, 989, 1935. ¹⁵) GOLDENBERG et al., *Amer. J. Med.*, **5**, 792, 1948. ¹⁶) BARCROFT and KONZETT, *J. Physiol.*, **110**, 194, 1949. ¹⁷) SWAN, H. J. C., *Lancet*, **2**, 508, 1949. ¹⁸) KAPPERT et al., *Acta cardiol.*, **5**, 121, 1950. ¹⁹) BEARN et al., *18th International Physiology Congress*, Copenhagen, 1950. ²⁰) BARNETT et al., *Clin. Sci.*, **9**, 151, 1950. ²¹) GOLDENBERG et al., *Arch. intern. Med.*, **86**, 823, 1950. ²²) CORY and BUCHWALD, *Amer. J. Physiol.*, **95**, 71, 1930. ²³) REIN, H., *Physiologie des Menschen*, Berlin, 1949; MADISON, L. L., *J. clin. Invest.*, **29**, 689, 1950. ²⁴) For a review, see GRIFFITH, F. R., jr., *Physiol. Rev.*, **31**, 151, 1951. ²⁵) MOYER et al., *Circulation*, **5**, 91, 1952. ²⁶) WAKIM and ESSEX, *ibid.*, **5**, 370, 1952.

Insulin

Chemistry

Protein of mol. wt. ca. 6000, soluble in water, insoluble in most organic solvents, fairly easily decomposed. The structure of insulin has recently been elucidated by SANGER and co-workers¹, who have shown that the fundamental molecular unit consists of two polypeptide chains built up respectively of 21 and 30 amino-acid residues and joined by the disulphide bridges of 3 cystine residues. The amino-acid sequences have been determined for ox, pig and sheep insulins, and show slight differences reflected in differences in the mol. wt. (5734, 5778 and 5704 respectively).

Unit

International unit for simple standardized insulin = 0.0454 mg cryst. insulin (1 mg cryst. insulin = 22 I.U.). The international insulin unit is that quantity of insulin which lowers the blood sugar of a 2-kg, 24-hour-starved rabbit to 45 mg/100 ml in 3 hours.

Methods of test and assay

Blood-sugar depression in rabbits (see Unit), convulsions in mice.

Physiology and function

Insulin is formed in the islet cells of the pancreas. The secretion is continuous (basal secretion 0.005–0.035 I.U./kg per hour ac-

cording to HOUSSAY, 1929) with variations which are regulated mainly by the blood-sugar level. The normal insulin level in blood amounts to between 6.25×10^{-5} and 6.25×10^{-4} I.U.².

Insulin deficiency² results *in vivo* in most species of animals in a series of symptoms, beginning with an increase in hepatic glycogenolysis and in elimination of sugar from the liver into the blood. As soon as the blood-sugar concentration exceeds the absorption capacity of the renal tubules glycosuria develops, entraining in turn an increase in water elimination. At the same time fat and protein metabolism increase, resulting in increased production of glucose (gluconeogenesis). These metabolic changes are accompanied by increased elimination of nitrogen, increased B.M.R., lowered respiratory quotient and inability to store exogenous sugar. The loss of water and calories in the urine and the increased fat and protein catabolism in the tissues result in the classical syndrome of polyuria, polydipsia and polyphagia. The increased diuresis causes further symptoms as a result of the changes in water and electrolyte metabolism. The fat catabolism eventually results in the formation of acetoacetic and β-hydroxy-butyric acids, ketonaemia and ketonuria. The accumulation of keto-bodies and the loss of electrolytes lead to metabolic acidosis

characterized by low bicarbonate content and low pH of the blood. This acidosis in turn causes further progressive metabolic disturbances as a result of accelerated breakdown processes in the tissues, characterized by liberation of inorganic phosphates and associated cations and their excretion in urine. The continuous loss of electrolytes results in a dehydration due to diminished capacity to retain water. The results are haemoconcentration, diminished total blood volume, lowered blood pressure and finally collapse of the peripheral blood circulation and renal function with resultant shock³. The toxic effect of the keto-bodies on the brain causes a reduction of the cerebral metabolism with lowered cerebral oxygen uptake, and finally loss of consciousness⁴.

The longstanding difference of opinion as to whether the hyperglycaemia of insulin deficiency is a result of lowered capacity to utilize sugar or of increased gluconeogenesis has been ended by recent researches using radio-isotopes which have shown that both processes are responsible^{5,6}.

The symptoms of insulin deficiency described above are the result of disturbances of the cell metabolism. The disturbances in the liver cells differ from those in the muscle cells and may be summarized as follows²:

Liver cells

1. Diminished capacity to utilize glucose owing to disturbance of the enzyme system responsible for the conversion of glucose into fructose 6-phosphate (*diabetics can utilize fructose*)^{7,8} with resulting diversion of glucose into the blood.
2. Diminished lipogenesis, again resulting in diversion of glucose into the blood.
3. Increased oxidation of fatty acids owing to their increased mobilization from reserves with resulting increase in C₂ degradation products. The latter are diverted to the synthesis

of acetoacetic acid and cholesterol and undergo oxidation in accordance with the KREBS cycle.

4. Increased oxidative deamination of the mobilized amino-acids with resultant increase in keto-acids available for the KREBS cycle.

Muscle cells

1. Diminished oxidation of active C₂ degradation products of pyruvates and acetates, compensated by increased oxidation of C₂ products of fatty acids and acetoacetates.
2. Diminution of oxidative phosphorylation due to the KREBS cycle, with resultant lowered availability of energy-rich phosphate combinations.
3. Lowered glucose uptake due to disturbance of the hexokinase reaction, with resulting decrease in gluconeogenesis.

It has not yet been established whether these multiple disturbances of liver- and muscle-cell metabolism are due to a multiple hormonal activity of insulin or are the multiple effects of one single process as yet unknown. On the other hand it is known that insulin regulates the cell metabolism in conjunction with other hormones and that the disturbances resulting from its absence are at least in part due to a reactionary increase in the activity of these co-regulators. Furthermore, overproduction of these co-regulators can result in diabetes without there being necessarily a complete lack of insulin. Hyperactivity of the adrenal cortex for example, accompanied by a (relative) pancreatic insufficiency, leads to diabetes, as also does hyperactivity of the anterior pituitary (cf. Growth hormone, pages 192 and 193). These forms of diabetes, particularly the pituitary form, are markedly insulin-resistant.

Therapeutic application

Insulin diabetes, loss of weight (stimulation of appetite), supporting therapy in lesions of the liver parenchyma, insulin shock.

¹) SANGER et al., *Biochem. J.*, **60**, 541, 1955; SANGER et al., *ibid.*, **60**, 556, 1955. ²) MIRSKY, A. J., *Recent Progr. Hormone Res.*, **7**, 437, 1952. ³) GUEST, G. M., *Amer. J. Med.*, **7**, 630, 1949. ⁴) KETY, S., *Proc. Amer. Diabetes Ass.*, **8**, 259, 1948. ⁵) FELLER et al., *J. biol. Chem.*, **187**, 571, 1950. ⁶) STETTEN et al., *ibid.*, **192**, 817, 1951. ⁷) PRICE, CORI and COLOWICK, *J. biol. Chem.*, **160**, 633, 1945. ⁸) CHAIKOFF and SCHUSDECK, *ibid.*, **194**, 435, 1952. ⁹) GROEN et al., *J. clin. Invest.*, **31**, 97, 1952. For reviews, see STADIE, W. C., *Physiol. Rev.*, **34**, 52, 1954, and LEVINE and GOLDSTEIN, *Recent Progr. Hormone Res.*, **11**, 343, 1955. On diabetes and insulin, see also BEST, C. H., *Diabetes and Insulin*, Springfield, 1948.

Parathyroid hormone

The hormone of the parathyroid is a protein which appears to possess no prosthetic group and does not belong to the glycoproteins. It is sparingly soluble in water, insoluble in acetone, ether and pyridine, easily soluble in weak hydrochloric acid and 80% alcohol.

Unit

COLLIP unit = $\frac{1}{100}$ of the quantity which raises the blood-calcium level in dogs by 5 mg/100 ml.

Methods of test and assay

Increase of the blood-calcium level in dogs (carnivores are markedly more sensitive to parathyroid hormone than vegetarians).

Physiology and function

Parathyroid hormone has two points of attack: the kidneys (increase of phosphorus elimination) and the bones (calcium mobilization). It thereby regulates calcium metabolism, together with vitamin D but with greater effect and by a different mechanism (vitamin D mobilizes the calcium of the soft tissues, contributes to the conversion of organic serum phosphorus into inorganic P and improves the body's calcium supply by promoting resorption). In the treatment of hypoparathyroid conditions it is therefore possible to replace vitamin D by parathyroid hormone or even better by dihydrotachysterol (A.T. 10) which is obtained by reduction of vitamin D₂ (the mechanism of action of A.T.10 is not the same, however, as that of vitamin D).

Therapeutic application

In hypoparathyroid conditions (alternatively dihydrotachysterol, see Vitamin D, page 210).

Thyroxine

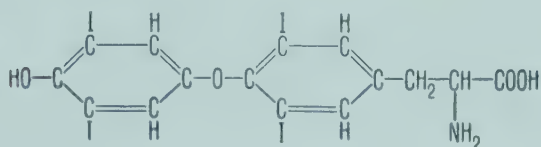
The normal thyroid gland contains 0.007–0.18% iodine, i.e. about 20% of the total iodine content of the body. The thyroid iodine is 90% combined in the form of a protein complex, the thyroglobulin, which contains both thyroxine and its precursor di-iodotyrosine. Thyroxine is the 4-hydroxy-3:5-di-iodophenyl ether of di-iodotyrosine. It is easily soluble in 90% alcohol and in

alkalis, insoluble in water and acids. The natural (–)-thyroxine present in the body is biologically about 3 times more active than the DL-thyroxine isolated from the gland or the synthetic (+)-thyroxine (the racemization during isolation is apparently due to the process used).

Thyroxine, $C_{15}H_{11}O_4NI_4$

Mol. wt. 776.93

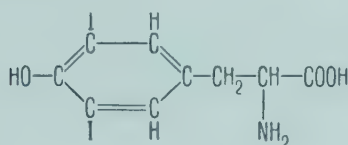
M. p. 232–233°C

crystallizes in rosettes of colourless needles
tasteless and odourless**Di-iodotyrosine** (no hormonal effect), $C_9H_9O_3NI_2$

Mol. wt. 433.01

M. p. 204°C

crystallizes in prisms

**Methods of test and assay**

Chemically (iodometrically) or biologically (by effect on the metamorphosis rate of larvae of amphibia or by increase in B.M.R. in rats).

Physiology and function

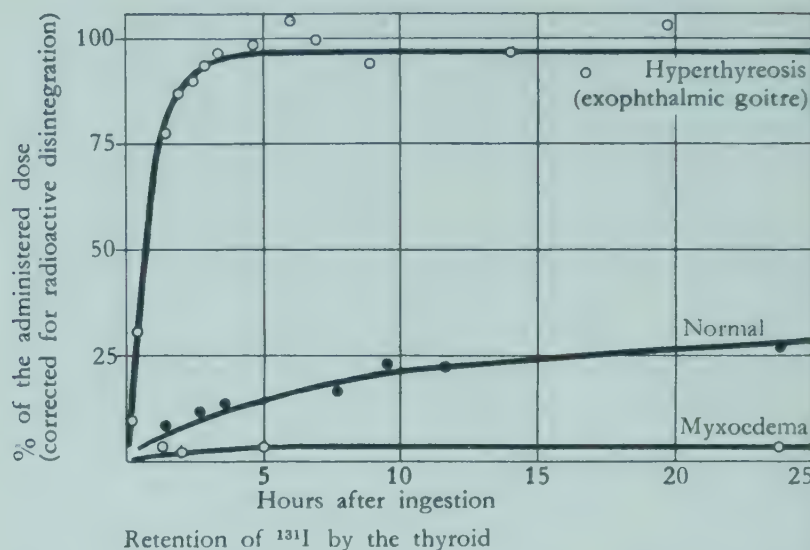
It has been shown by TAUROG and CHAIKOFF¹ that the thyroid hormone circulating in the blood is identical with thyroxine. The route of the biochemical synthesis previously assumed, from tyrosine via the mono- and di-iodo-derivatives, has now been confirmed by means of radioactive tracers².

When there is excess iodine in the blood the thyroid retains only a small percentage, the rest being eliminated in urine (ca. 37%) and in faeces (ca. 17%)³. Small iodine doses on the other hand are accepted by the thyroid up to 65%⁴.

The circumstance that a large part of the bodily iodine is stored by the thyroid makes possible one of the few applications of radioactive isotopes of importance in diagnosis and therapy. For example, a test dose of 100 microcuries of I-131 provides a simple method for evaluating thyroid activity which is now also the most reliable. The quantity of iodine retained by the thyroid is quite simply measured by measuring its radioactivity with the aid of a GEIGER counter⁵. By this method typical retention curves are obtained for hyper-, normal or hypo-activity of the thyroid (see diagram)⁶. The distribution of the radioactive iodine in the gland tissues (from radiographs of microtome slices of surgically removed material) provides information on the nature of thyroid tumours, in particular in cancer. In the latter case the radiographs show whether the tumour or metastases consist of functioning gland tissue and thus whether they are amenable to radio-iodine therapy (cf. the outstanding work of MARINELLI⁷). The treatment of BASEDOW's disease by radio-iodine is now the preferred method in cases where surgical treatment is useless or impossible.

Orally thyroxine is about 20%, its salts about 45%, less effective than dried thyroid preparations (or thyroglobulin); subcutaneously they are fully effective. Dried thyroid preparations are equally effective orally and subcutaneously. Thyroactive substances are not eliminated in urine⁸.

The action of thyroxine consists in an increase in general metabolism and takes place at the cell level. Fat, carbohydrate and protein metabolism are equally affected. The blood circulation,



water balance, cerebral centres and gonads are also affected, presumably secondarily.

Iodine, di-iodotyrosine and di-iodothyronine indirectly inhibit the activity of the thyroid since high iodine levels in blood cause the pituitary to lower the liberation and/or production of the thyrotropic hormone and thereby the thyroid activity. As a consequence these substances appear to be antagonists of thyroxine. In fact, however, administration of thyroxine has the same result; the inhibition of thyroid activity is merely masked by the exogenous thyroxine, i.e. by the hormonal symptoms which the latter produces.

The action of thyrotropic hormone on the thyroid consists mainly in an increased discharge of thyroxine and in a stimulation of the hormone-producing epithelium. Shortage of thyrotropic hormone leads to increased storage of colloids and to flattening of the epithelium.

The individual sensitivity to thyroxine varies greatly from person to person; the consumption of meat tends in general to increase the sensitivity.

There is a certain antagonism between vitamin C and thyroxine, while vitamin D acts synergistically.

Between vitamin A metabolism and thyroxine there is also a definite but unexplained connection in that during thyroxine shortage (in cretinism, myxoedema or due to thiouracil) the organism can no longer convert carotenes into vitamin A (high level of carotenes in blood in myxoedema). Vitamin A itself, however, can be taken up normally by the body during thyroxine shortage⁹.

Thiourea, thiouracil, thiocyanates, 1-5-vinyl-2-thio-oxazolidone (in cabbage and kohlrabi)¹⁰, as well as certain sulphonamides, suppress the activity of thyroxine. The exact point of attack is unknown but the mode of action is as follows: the capacity of the thyroid to combine iodine is inhibited and it produces thyroxine only in very small quantities. The diminished thyroxine level in blood provokes an increased production of thyrotropic hormone, which leads to hyperplasia of the thyroid and in extreme cases to goitre. – A similar mechanism is associated with endemic goitre, in which the iodine deficiency of the thyroid is exogenous.

Therapeutic application

Hypothyreosis, thyrogenic adiposity, disturbances of development and growth, polyglandular insufficiency, fractures.

¹) TAUROG and CHAIKOFF, *J. biol. Chem.*, **171**, 439, 1947. ²) LEBLOND, C. P., *Advanc. biol. med. Phys.*, **1**, 353, 1948. ³) PERLMAN, CHAIKOFF and MORTON, *J. biol. Chem.*, **139**, 433, 1941. ⁴) HAMILTON and SOLEY, *Proc. nat. Acad. Sci.*, **26**, 483, 1940. ⁵) BERSON et al., *J. clin. Invest.*, **31**, 141, 1952. ⁶) WASSERMANN and LOEVINGER, *Advanc. intern. Med.*, **4**, 118, 1950. ⁷) MARINELLI et al., *Amer. J. Roentgenol.*, **58**, 17, 1947. ⁸) MONROE, R. A., *Thesis, University of Ann Arbor, Mich.*, 1949. ⁹) Editorial, *J. Amer. med. Ass.*, **137**, 91, 1948. ¹⁰) ASTWOOD, GREER and ETTINGER, *J. biol. Chem.*, **181**, 121, 1949.

For bibliographical sources of this section, see footnote on page 215

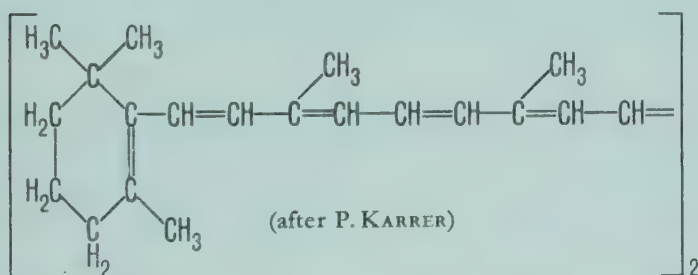
Vitamin A

Vitamin A occurs naturally in three or more forms (vitamers) either as alcohol or the derived esters. It is found only in the animal organism. Crystalline A vitamers are pale yellow to yellow in colour, fat-soluble, insoluble in water. They are easily oxidized, but in the absence of oxygen are stable to alkalis, acids and heat.

The A vitamers do not occur in the vegetable kingdom but only their precursors, the carotenes, which are converted by the animal organism into vitamin A. The average useful biological effect of this conversion is expressed by: activity of 2 parts of carotenes = activity of 1 part vitamin A (see Units). Of the nine known carotenes those most important for the animal organism are α -, β - and γ -carotene and cryptoxanthin, of which β -carotene is the most active biologically.

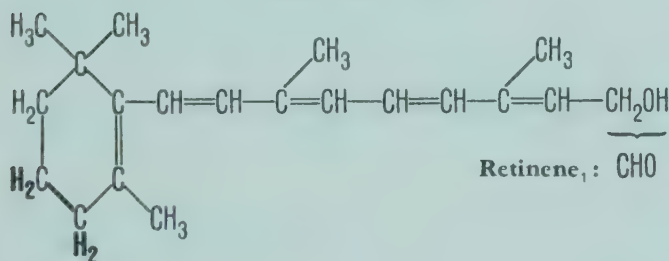
β -Carotene, $C_{40}H_{56}$

Mol. wt. 536.85
Red crystals
M. p. 187 °C
Absorpt. max. 4540 Å



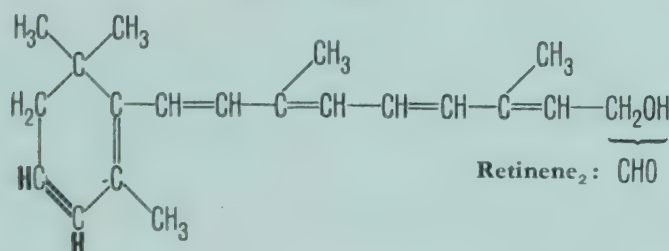
Vitamin A₁, $C_{20}H_{30}O$, from liver of salt-water fish

Mol. wt. 286.44
M. p. 8 °C
Absorpt. max. 3280 Å



Vitamin A₂, $C_{20}H_{28}O$, from liver of fresh-water fish

Mol. wt. 284.42



Units

Vitamin A:

1 internat. unit (I.U.) = 0.0003 milligram vitamin A alcohol
= 0.00034 milligram vitamin A acetate

1 British unit = 1 U.S. Pharmacopeia unit = 1 international unit

Carotenes:

1 international unit = 0.0006 milligram β -carotene, equal in activity to 1 I.U. vitamin A.

Methods of test and assay

Spectrophotometrically (B.P.) or colorimetrically. In Great Britain and USA the official method for pharmaceuticals is the growth test on A-deficient rats. Carotenes colorimetrically after chromatographic separation; CARR-PRICE test.

Occurrence (values are in I.U. of vitamin A per 100 g weight fresh)

Vitamin A: fish-liver oils (halibut) 2–4 millions, (tunny) 0.5–8 millions, (cod) 100,000; sardines 4800–54,000.

Carotenes: palm oils 50,000–500,000; parsley 18,000; dandelion leaves 12,000; spinach 9000.

Vitamin A + carotenes: calf liver 50,000–500,000; liver of other domestic animals 12,000–40,000; egg-yolk (dark yellow) 2900; cow's milk (winter) 500, (summer/autumn) 1000; human milk 150–160, colostrum 600.

Physiology

Carotenes. The carotenes are widely distributed throughout the vegetable kingdom and can be converted into vitamin A by most animals (with the exception of the pure carnivores such as cats). In accordance with the constitutional formula one molecule of β -carotene yields two molecules of vitamin A₁. Biologically, however, the yield is much lower; thus cryst. vitamin A₁ acetate is 4 times as active and vitamin A in fish-liver oil twice as active, weight for weight, as cryst. β -carotene (tested on growth of chicks)¹. The conversion takes place in the small intestine² and the yield is increased in the presence of vitamin E. *In athyreosis (cretinism, myxoedema) the organism is no longer capable of converting carotenes into vitamin A³; in other diseases, particularly those of the liver, kidneys and intestine, diabetes and phosphorus poisoning, the capacity for conversion is greatly diminished. Young children and infants are also only capable of converting carotenes into vitamin A in limited quantities.*

Apart from the above limitations it is to be noted that the resorption of carotenes from vegetable foodstuffs is relatively poor, e.g. a maximum of 20% of the total carotene present in carrots, in the case of green vegetables somewhat more.

The liver stores considerably more vitamin A when the latter is consumed as such, as when it is consumed in the form of carotenes. The organism appears to limit its conversion of carotenes in accordance with its day to day requirements of vitamin A.

The carotene level in blood varies greatly with the nature of the nutriment absorbed and amounts on the average to 200–300 μ g per 100 ml plasma. It is increased physiologically in pregnancy (parallel with the vitamin E level)⁴ and pathologically in cretinism, myxoedema and diabetes.

Vitamin A. The resorption of vitamin A from natural fatty media, in which it occurs mainly in the form of esters, takes place efficiently and rapidly in the presence of bile (ca. 80%), the blood level reaching a maximum about 3–5 hours after intake. The resorption of the water-soluble preparations of vitamin A, such as the cryst. acetate or the pure vitamin (alcohol)⁵, is even better, the latter being the most rapidly absorbed. The average blood level amounts to 100–300 I.U./100 ml serum, the level being lower in winter. In pregnancy a low level in the mother is often accompanied by a higher level in the foetus; the latter, however, is largely independent of the former and never exceeds the normal figure.

Vitamin A is stored principally in the liver (ca. 22,000 I.U. per 100 g) but also in the lungs, kidneys, gonads and adrenals; in other organs only in traces. The vitamin-A content of the liver falls ca. 50% in hypertonia, ulcers, coronary thrombosis, tuberculosis, syphilis, endocarditis, more in cardiovascular and septic diseases, and is at its lowest in chronic nephritis and gallbladder and kidney infections.

In the healthy body vitamin A is not eliminated from the kidneys, in disease the elimination can reach 3000 I.U. per day (maximum in pneumonia).

Owing to the high vitamin-A storage level in the liver a deficiency in the nutriment is only slowly reflected in the body. Initially there is a rather rapid disappearance of carotenes from the plasma but the vitamin-A plasma level is maintained up to 2 years⁶. The same studies⁶ showed that the daily vitamin-A requirement in health is 2500 I.U. or in the form of carotenes 4000 I.U. in oily solution, 7500 I.U. in green vegetables, 12,000 I.U. in cooked carrots.

Function

The carotenes as such have no vitamin function.

Nothing is known in detail of the role of vitamin A in cell metabolism. It is certain that it plays a fundamental role in the visual process in the rhodopsin (visual purple) cycle^{7, 10}, together with the vitamins B₂, nicotinic acid and possibly E (vitamin A₁ aldehyde = retinene₁; vitamin A₂ aldehyde = retinene₂) and that it is of importance in the cell metabolism of the epithelial tissues.

Vitamin A promotes growth and has a diuresis-promoting effect on the kidneys. It also appears to have a specific effect on the thyroid (predisposition to or development of goitre in A-deficiency).

Vitamin A also affects the development of the teeth: during the active development and calcification phase vitamin-A deficiency leads to degenerative changes in the specialized tooth-forming cells, resulting in hypoplasia of the eventual tooth substance⁹.

Toxicology

In large doses vitamin A can have a toxic effect. For this reason the liver of the polar bear and polar fox is poisonous to man. A-Hypervitaminosis has been observed in young children after protracted treatment with high doses (e.g. 200,000 I.U. daily for 6 months). The first symptoms are restlessness, irritability, dis-

inclination to standing, pruritus, then loss of appetite, swellings over various bones, falling hair; temperature, blood-picture and -sedimentation remain normal. The swellings are either of soft tissues over the bones or hyperostoses. – After cessation of vitamin-A administration the symptoms disappear rapidly and the hyperostoses are reabsorbed⁸.

Therapeutic application

Prophylactic: in illness of long duration, in which the resorption, conversion or storage is affected (hepatopathy, obstruction of the bile duct, athyreosis, hypothyreosis, intestinal complaints, diabetes, kidney troubles).

Curative: defective scotopic vision, night-blindness (not always due to A-deficiency), xerophthalmia, cutaneous and mucous infections, hyperkeratosis.

¹⁾ GURCAY et al., *J. Nutr.*, **41**, 565, 1950. ²⁾ THOMPSON et al., *Brit. J. Nutr.*, **3**, 50, 1949. ³⁾ Editorial, *J. Amer. med. Ass.*, **137**, 91, 1948. ⁴⁾ DARBY et al., *Ann. N. Y. Acad. Sci.*, **52**, 328, 1949. ⁵⁾ KAYAN et al., *J. Nutr.*, **40**, 275, 1950, and WEEK and SEVIGNE, *ibid.*, **40**, 563. ⁶⁾ Report of the Vitamin A Sub-Committee of the Accessory Food Factors Committee, *Spec. Rep. Ser. Med. Res. Coun. (Lond.)*, No. 264, 1949. ⁷⁾ WALD, G., *Science*, **109**, 482, 1949, and WALD and HUBBARD, *J. gen. Physiol.*, **32**, 367, 1949. ⁸⁾ CAFFEY, J., *Pediatrics*, **5**, 672, 1950, and CAFFEY, J., *Pediatric X-Ray Diagnosis*, Chicago, 1950, p. 747. ⁹⁾ DINNERMAN, M., *Oral Surg. Oral Med. Oral Path.*, **4**, 1024, 1951. ¹⁰⁾ WALD, G., *Ann. Rev. Biochem.*, **22**, 497, 1953.

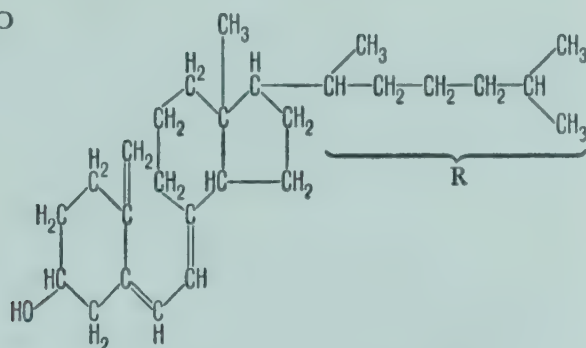
Vitamin D

Of this group only vitamin D₃ occurs naturally in the higher animals. It is formed photochemically from 7-dehydrocholesterol. Other substances with D-activity and of known chemical structure, D₂ (calciferol), D₄ and D₅, are artificially produced by irradiation of ergosterol, of 22-dihydroergosterol and of 7-dehydro-sterol respectively. These artificial vitamin-D compounds have not yet been identified in animals.

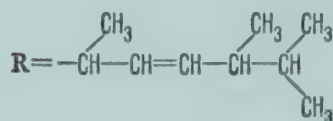
D₂ or calciferol was formerly erroneously regarded as the natural vitamin on account of the similarity of its absorption band with that of D₃. D₂ is distinguished chemically from the natural vitamin D₃ by its unsaturated side-chain, pharmacologically by its somewhat greater toxicity, biologically by its different antirachitic effect in various animal species (in rats the same, in chickens and apes less effective), by its *antirachitic ineffectiveness when administered parenterally*³ and by the fact that its precursor, ergosterol, is not absorbed in the animal intestine. When administered orally in man D₂ and D₃ exhibit no difference in their antirachitic effect. In addition to D₃ other D-vitamins of unknown structure and of considerably greater antirachitic effect are known to be present in fish-liver oils.

D₃, D₂, D₄ and D₅ are odourless crystalline compounds, soluble in fats and fat solvents, insoluble in water, not readily oxidized. They have a common absorption band at ca. 2650 Å and cannot therefore be distinguished spectroscopically.

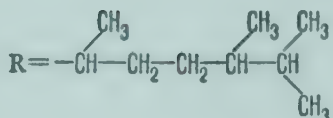
Vitamin D₃, C₂₇H₄₄O
Mol. wt. 384.62



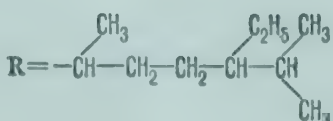
Vitamin D₂, C₂₈H₄₄O
Calciferol
Mol. wt. 396.63



Vitamin D₄, C₂₈H₄₆O
Mol. wt. 398.5



Vitamin D₅, C₂₉H₄₈O
Mol. wt. 412.4



Units

Vitamin D₃:

1 international unit = 0.000025 milligram cryst. vitamin D₃.

1 British Pharmacopoeia unit = 1 U. S. Pharmacopoeia unit = 1 international unit.

Vitamin D₂:

1 international unit = 1 milligram of the international standard preparation of irradiated ergosterol (in solution in a vegetable oil).

Methods of test and assay

Antirachitic test on rats (official test in Great Britain and USA for pharmaceuticals and foodstuffs).

Occurrence (values are in I.U. per 100 g weight fresh)

Fish-liver oils (tunny) 1.6–25 millions, (halibut) 20,000–400,000 (cod) 8000–30,000; egg-yolk 300; human milk (summer) 2.4–3.8, (winter) 0.3–1.7.

Physiology and function

In man the vitamin is formed by the action of the sun's rays in the outermost layers of the skin, in furred animals and birds in the fur or feathers, whence it reaches the organism through grooming or licking or by direct resorption. The origin of vitamin D in fish is unknown. As with all the fat-soluble vitamins bile is necessary for resorption; in the body it is partly destroyed (mechanism unknown) and partly eliminated via the intestine; the urine in health contains no vitamin D.

In children and adults the blood level amounts to 66–165 I.U. per 100 ml with seasonal variations; with a daily administration of 50,000–500,000 I.U. the blood level in adults rises to 9000 to 13,000 I.U./100 ml.

Vitamin D regulates the calcium and phosphorus balance by direct action on the phosphorus metabolism. It mobilizes the phosphorus from the soft tissues and contributes to the conversion of organic into inorganic phosphorus and to phosphorus metabolism during muscular work. Through its regulation of phosphorus metabolism vitamin D controls the calcium metabolism, on the one hand by promotion of calcium resorption, on the other hand by making possible, through the conversion of organic into inorganic phosphorus, the formation in the blood of the calcium phosphate necessary for bone development. Balanced and sufficient calcium and inorganic phosphorus concentrations in blood therefore lower the vitamin-A requirement and vice versa.

Toxicology

All D-vitamins, both natural and artificial, can be toxic in excessive doses; in most cases, however, 10,000 I.U. per kilogram body weight can be tolerated. With high doses vitamin D has the opposite effect, the bones becoming decalcified and the soft tissues calcified. The renal tubules, the media of the renal arterioles and the large vessels are particularly endangered.

Symptoms of vitamin-D poisoning: initially, increased buoyancy and appetite (tonic effect), followed by loss of appetite and proportionally greater loss of weight, nausea, headache, joint pains, profuse sweating, diarrhoea, marked increase in urinary calcium and phosphorus, increase in blood calcium, polydipsia, polyuria, progressive damage to the kidneys (albuminuria, increase of non-protein nitrogen in blood).

On cessation of D-administration the symptoms usually disappear rapidly; the calcifications are also reversible if the damage to the tissues has not proceeded too far. Vitamin B₁ increases the tolerance for D. Reduction of the calcium intake in food is useless since the bone calcium is mobilized.

Therapeutic application

Prophylaxis of rickets: sun-baths, quartz-lamp irradiation, fish-liver oil or pure vitamin (400 I.U. per day; in premature births 800–1500 I.U. Prophylaxis of rickets by shock doses of vitamin D is not recommended on account of its dangers. Cf. review of vitamin-D intoxications by CHAPLIN et al. in *Amer. J. med. Sci.*, **221**, 369, 1951), diet rich in vegetables, limitation of cereals since

the phytic acid¹ contained in these forms an insoluble compound with calcium not absorbable in the intestine², limitation of cow's milk.

In *elderly persons*, for remedying the calcium loss which increases with age (in the aged on a diet rich in starch and sugar a daily calcium loss of ca. 100 mg has been observed).

In *rickets* and *infantile tetany* (spasmophilia). In osteomalacia; in acute *lead poisoning* together with calcium for rapid immobilization in the bones of the lead in the blood stream, and subsequent dispersal by parathyroid hormone.

For treatment of *lupus vulgaris*, 50,000 I.U. 3–4 times daily. Contraindicated in kidney troubles, arteriosclerosis. Control of non-protein nitrogen and blood calcium level. See also footnote³.

After-treatment of hypoparathyroidism: If the condition has returned to normal after treatment with dihydrotachysterol (A.T. 10), vitamin D 50,000 I.U. 3 times weekly can be administered. A.T. 10 is, however, to be preferred if the higher cost permits it. (Dihydrotachysterol is closely related to vitamin D. It is obtained by reduction of vitamin D₂, but has no antirachitic activity.)

¹) When sufficient exposure to the sun occurs the decalcifying action of phytic acid is not observed (WALKER, A. R. P., *Lancet*, **2**, 244, 1951).

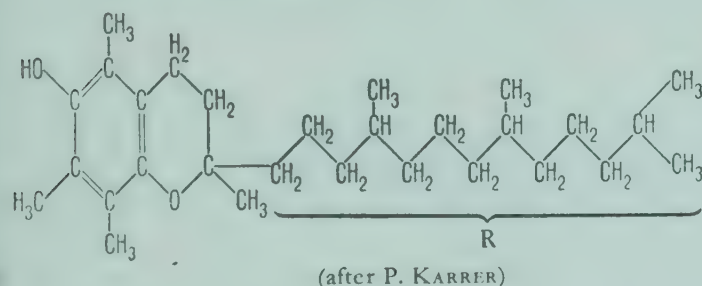
²) Phytic acid is largely destroyed in yeast fermentation, so that yeast bread can be prescribed.

³) In *lupus vulgaris* the therapeutic effect of D₂ is the same whether administered parenterally or orally, so that if the latter method causes toxic symptoms it may without hesitation be replaced by the former; some cases may require parenteral administration from the start.

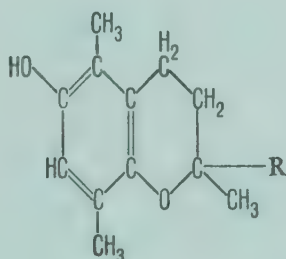
Vitamin E

Vitamin E occurs naturally in three different forms, α -, β - and γ -tocopherol, of which α -tocopherol is biologically the most active. All three vitamers are viscous oils insoluble in water; in the absence of oxygen they are stable to heat, acids and (visible) light, unstable to ultraviolet light, alkalis and oxidation. The tocopherols are antioxidants but are rapidly decomposed in rancid fats. The esters are more stable than the free alcohols and in many cases have the same biological effect. – The tocopherols occurring in wheat-germ oils are remarkably stable. Vitamin E is not destroyed by cooking.

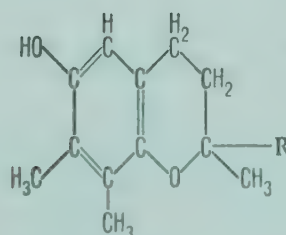
α -Tocopherol, C₂₉H₅₀O₂
Mol. wt. 430.69



β -Tocopherol, C₂₈H₄₈O₂
Mol. wt. 416.66



γ -Tocopherol, C₂₈H₄₈O₂
Mol. wt. 416.66



Unit

1 international unit (I.U.) = 1.0 milligram of synthetic racemic α -tocopherol acetate. (The biological activity of synthetic racemic α -tocopherol is ca. 30% less than that of the natural product.)

Methods of test and assay

Rapid determination: FARBER et al., *Fed. Proc.*, **10**, 294, 1951.

Microchemically: QUAIFFE et al., *J. biol. Chem.*, **180**, 1229, 1949.

Other methods of determination: QUAIFFE et al., *J. biol. Chem.*, **156**, 499, 1944; *ibid.*, **159**, 663, 1945.

Occurrence (values are in mg per 100 g)

Wheat-germ oil 320; cottonseed oil, refined, 83–92; arachis oil 26–36; wheat germ 27; wholemeal wheat flour 1.2–3.4; widespread in green plants.

Physiology and function

Nothing certain is known of the biochemistry of vitamin E. Studies *in vitro* and *in vivo* indicate that it must play a part in various enzyme systems, particularly in protein metabolism. In the organism it has an influence on vitamins A and C, although there is no correlation between the requirements. This effect is perhaps connected with the antioxidant properties of vitamin E.

Experiments on animals have yielded the following results:

In rats vitamin-E deficiency brings about creatinuria, degenerative changes in muscles and nerves, decrease of cholinesterase in plasma, liver and brain, lowered resistance to poisoning and to protein-deficient diet; in male rats it causes atrophy of the testes reversible only in the early stages and aspermatogenesis, in female rats resorption sterility. The symptoms vary from species to species. For example, E-deficiency in the female mouse causes resorption sterility as in the rat, while in the male mouse spermatogenesis remains unaffected. In monkeys E-deficiency causes creatinuria (120 mg/day), 6 times greater elimination of allantoin, muscle dystrophia and leucocytosis⁶.

Recent studies have shown that vitamin E exercises a definite protective action against necrosis and fatty degeneration of the liver under qualitatively protein-deficient diets in the rat (in this case amenable to methionine treatment)³, against poisoning by highly unsaturated fatty acids (liver oils: rat, chicken)³, carbon tetrachloride⁴, alloxan⁵ (rats), etc.

The fatty degeneration of the liver in CCl₄-poisoning is amenable to vitamin-E (or protein) treatment only during the first 24 hours after the poisoning, subsequently it can be successfully treated with vitamin B₁₂ which also has a favourable influence on liver regeneration even in the very late stages¹.

In man:

Attempts to apply vitamin E usefully to the human organism, in analogy with its unequivocal effects in animals, have produced merely inconclusive and contradictory results; the significance of vitamin E for man remains as yet unexplained, although its occurrence in all the bodily tissues indicates that its role must be important.

In the tissues vitamin E occurs in concentrations of 0.1–1.1 mg per gram fat (highest concentration in the fat of uterus and testes). The plasma level⁷ amounts on an average to 1 mg/100 ml (range 0.5–1.5 mg, 200 samples). In illness involving lowered fat re-sorption the E-content of the plasma is diminished; it shows no variation in the menstrual cycle but is physiologically increased during pregnancy (parallel to the carotene content); in illness involving cholesterolaemia it shows an increase. – 90% of the vitamin E in the human organism consists of α -tocopherol.

Therapeutic application

In view of the contradictory reports in the literature therapy must necessarily be tentative: in muscular disturbances, such as progressive muscular dystrophy and amyotrophic lateral sclerosis (very little or no success; it is not certain that the favourable effect can be ascribed to vitamin E in view of the fact that wheat-germ

oil, which contains other substances of unknown activity, is usually used. Cf. the reviews of BICKNELL⁸ and others⁹); in diabetes (recommended by VOGELSANG¹⁰ and BUTTURINI¹¹, disputed by GUEST¹² and BENSLEY et al.¹³); in angina pectoris (recommended by SHUTE¹⁸, disputed by TRAVELL et al.¹⁴, EISEN and GROSS¹⁵, RAVIN and KATZ¹⁶, BAER et al.¹⁷); in venous obstruction and the resultant ulceration and dermatitis, in burns (massive dosage, recommended by SHUTE¹⁸, STRITZLER¹⁹, disputed by PENNOCK²⁰); in peripheral arteriosclerosis, in intermittent claudication, in thromboangiitis obliterans (recommended by SHUTE¹⁸, BOYD et al.²¹, HALL RATHCLIFFE²², disputed by PENNOCK²⁰, LIPPMAN²³); success has also been reported in various collagen diseases, in SYDENHAM's chorea²⁴, in multiple sclerosis²⁵, and in menopausal disturbances (flushing and sweating) when oestrogens are contraindicated²⁶.

The effect of vitamin E as adjuvant in liver therapy has not yet been reported upon.

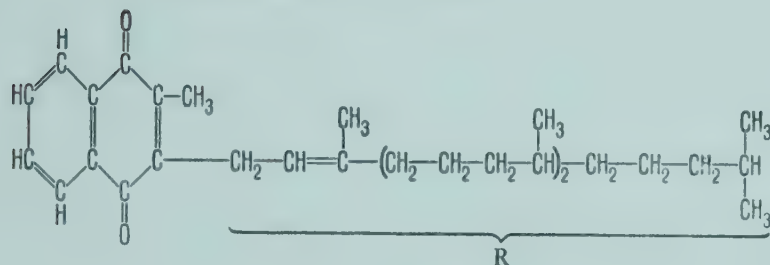
¹) HOVE and HARDIN, *Proc. Soc. exp. Biol.*, **78**, 858, 1951. ²) HIMSWORTH and LINDAN, *Nature*, **163**, 30, 1949; MATET et al., *C. R. Soc. Biol.*, **143**, 235, 1949; MOORE, T., *Ann. N. Y. Acad. Sci.*, **52**, 206, 1949; SCHWARZ, K., *ibid.*, 225. ³) DAM, H., *Ann. N. Y. Acad. Sci.*, **52**, 195, 1949; DAM, H., *Abstracts 1st Int. Congr. Biochem.*, 61 (Cambridge, England). ⁴) HOVE, E. L., *Ann. N. Y. Acad. Sci.*, **52**, 217, 1949. ⁵) GYÖRGY and ROSE, *ibid.*, 231. ⁶) DINNING et al., *Fed. Proc.*, **10**, 380, 1951. ⁷) DARBY et al., *Ann. N. Y. Acad. Sci.*, **52**, 328, 1949. ⁸) BICKNELL, F., *Int. Z. Vitaminforsch.*, **21**, 313, 1949. ⁹) McEACHERN and RABINOWITCH, *Advanc. intern. Med.*, **4**, 201, 1950. ¹⁰) VOGELSANG, A., *Ann. N. Y. Acad. Sci.*, **52**, 406, 1949. ¹¹) BUTTURINI, U., *ibid.*, 397. ¹²) GUEST, G. M., *ibid.*, 411. ¹³) BENSLEY et al., *Canad. med. Ass. J.*, **61**, 260, 1949. ¹⁴) TRAVELL et al., *Ann. N. Y. Acad. Sci.*, **52**, 345, 1949. ¹⁵) EISEN and GROSS, *ibid.*, 352. ¹⁶) RAVIN and KATZ, *New. Engl. J. Med.*, **240**, 331, 1949. ¹⁷) BAER et al., *Ann. N. Y. Acad. Sci.*, **52**, 412, 1949. ¹⁸) SHUTE, E. V., *ibid.*, 358. ¹⁹) STRITZLER, C., *ibid.*, 368. ²⁰) PENNOCK, L. L., *ibid.*, 413. ²¹) BOYD et al., *Lancet*, **2**, 132, 1949; ²²) HALL RATHCLIFFE, A., *Lancet*, **2**, 1028, 1949. ²³) LIPPMAN, H. I., *Ann. N. Y. Acad. Sci.*, **52**, 362, 1949. ²⁴) DOWD, G. C., *ibid.*, 419. ²⁵) DOWD, G. C., *ibid.*, 422. ²⁶) MACLAREN, H. C., *Brit. med. J.*, **2**, 1378, 1949.

Vitamin K

Vitamin K occurs naturally in at least two forms (K_1 and K_2) and many synthetic compounds are known which are chemically related to this vitamin and have similar activity. The K-vitamins are fat-soluble, fairly stable to heat, unstable to alkalis and light. Menadione (2-methyl-1:4-naphthaquinone), the most active of the synthetic products, has twice the activity of the natural vitamin and is more stable. Together with its many water-soluble derivatives it has therefore long since largely replaced the natural vitamin in clinical practice. Today, however, the importance of the natural vitamins, above all K_1 , has been reasserted as a result of the discovery that K_1 is by far the most rapid antidote to dicumarol and its derivatives (see below).

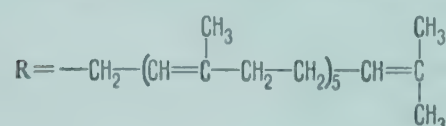
Vitamin K_1 , $C_{31}H_{46}O_2$

Mol. wt. 450.68
M. p. – 20 °C
Yellowish oil,
originally obtained from lucerne



Vitamin K_2 , $C_{41}H_{56}O_2$

Mol. wt. 580.86
M. p. 53.5–54.5 °C
Yellow crystals,
originally obtained from putrefying fish meal



Menadione, $C_{11}H_8O_2$

Mol. wt. 172.17
M. p. 106 °C
Yellow crystals

R = H

Units

No international unit, but 1 milligram of synthetic menadione has been proposed as such. 0.0008 mg menadione = 20 DAM

units = 1 ANSBACHER unit = the minimum quantity which in 6 hours normalizes the blood coagulation time of 70–100 g K-deficient chicks. There are in addition many other units which have no further significance now that the synthetic preparations permit definition by weight.

Methods of assay

Chemically (based on the reduction of the quinone group to hydroquinone); spectrometrically in pure solutions of K_1 , K_2 and menadione; best biologically on K-deficient chicks (see ANSBACHER unit).

Occurrence

Principally in green vegetables, above all in spinach, cabbage and Brussels sprouts. Moderate amounts in tomatoes and liver, very little in fruit, milk and meat.

Physiology and function

As in the case of all fat-soluble vitamins, fats and bile are necessary for the resorption of vitamin K and also of menadione, but not of the water-soluble synthetic preparations. – It is doubtful whether the consumption of vitamin K in food is at all necessary for the healthy adult since it is synthesized in considerable quantities by the intestinal bacteria (the concentration in the faeces is one of the highest of natural concentrations), although a number of alimentary K-avitaminoses have been described in the literature. In intestinal complaints it is impossible to decide whether the K-deficiency is due to changes in the bacterial flora or to decreased resorption of the vitamin intake.

The vitamin is stored in relatively small quantities in the liver, sufficient to meet the requirements of the body for only a week if there is no synthesis in the intestine and no exogenous source or a failure of resorption.

Climate has a definite influence on the K-balance since the requirement increases with rise in temperature.

Vitamin K is indispensable for normal blood coagulation since it plays an important part in the synthesis of prothrombin in the liver. Its exact role in the latter process is not yet known. It is not a component of prothrombin nor is it a likely intermediate product in the synthesis. Vitamin K has no direct effect on blood coagulation but probably acts via the liver or the prothrombin synthesis. The lowered blood prothrombin level following injury to the liver parenchyma can therefore only be influenced by vitamin K if the damage is not too advanced. No other functions have yet been discovered.

Vitamin K is an antagonist of dicumarol and its derivatives with respect to their prothrombin-lowering activity. Vitamin K₁ has the most rapid action, menadione the slowest. Intravenous instillation of a 5% (50 mg/ml) vitamin K₁ emulsion at the rate of 1 ml/minute to a total dose of 5–20 mg/kg body weight, or 360 to 1290 mg per patient, lowers prothrombin times of 43–85 seconds to 28–36 seconds in the space of 2 hours, and to 20–30 seconds in the space of 5 hours^{1,2}.

Therapeutic application

Prophylactic: for the prevention of haemorrhagic diatheses in the newborn, 2 mg menadione intramuscularly, intravenously or orally to the mother immediately (several hours) before the birth or to the infant after birth. Predisposition to bleeding in the

newborn is due to vitamin deficiency in the mother. During the first days of life and until such time as the intestinal synthesis commences, the infant is dependent on its initial reserve of vitamin K and on that in the breast milk. The intestinal synthesis usually starts at about one week.

Preoperative treatment of icteric patients. – In prolonged treatment with antibiotics which can have an eventual effect on the intestinal flora (tetracyclins, chloramphenicol).

Curative: (vitamin K₁) in all prothrombinopenic conditions due to deficiency of K in food or to poor resorption (intestinal disturbances, deficiencies of biliary or hepatic function); in poisoning, e.g. by petrol (gasoline) or benzene, or overdoses in dicumarol, ethyl biscoumacetate or salicylate therapy.

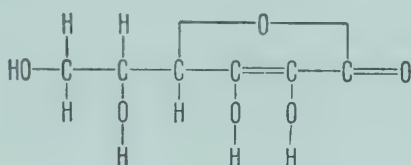
¹) COLLENTINE and QUICK, *Amer. J. med. Sci.*, **222**, 7, 1951. ²) WATKIN et al., *J. Lab. clin. Med.*, **37**, 269, 1951; for further references, see SHOSKES et al., *ibid.*, **36**, 531, 1950. Cf. also REID, R. A., *Quart. Bull. Northw. Univ. med. Sch.*, **25**, 292, 1951; FULLER and BARKER, *Minnesota Med.*, **34**, 326, 1951.

Vitamin C

Vitamin C occurs naturally in two forms, the one being the oxidation product of the other. Both forms are biologically active. They are water-soluble, insoluble in organic solvents, unstable to oxidation, light, alkalis and certain metals.

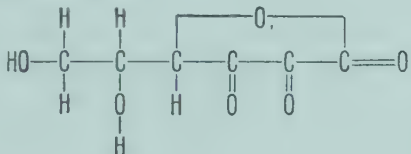
L-Ascorbic acid, C₆H₈O₆

Mol. wt. 176.12
White crystals
Acid taste
M. p. 190–192 °C



Dehydroascorbic acid (oxidized form)

C₆H₆O₆
Mol. wt. 174.11



reversible

Unit

1 international unit (I.U.) = 0.05 milligram cryst. L-ascorbic acid.

Methods of test and assay

Titration with N/100 iodine solution (B.P.) or 2:6-dichlorophenol/indophenol (in USA official method for pharmaceuticals and foodstuffs).

Occurrence (values are in mg per 100 g weight fresh)

Widely distributed in high concentrations, above all in green plants and citrus fruits. Parsley 154–209, dandelion leaves 100, peppers (green) 125–180, Brussels sprouts 87–150, currants 140, kohlrabi 60–117, lemon juice 30–78, orange juice 22–89, grapefruit juice 24–45.

Physiology and function

Vitamin C is to a certain extent stored in the body, particularly in the endocrine glands, also in the liver, spleen, brain, kidneys and heart. Muscle contains ca. 2 mg/100 g, mostly in stored fat, although it is not fat-soluble. It occurs in all body fluids. Blood level in health (plasma) 0.6–2.5 mg/100 ml; after injection of large doses, e.g. 1 gram, it rises to 250 mg, falls in 15 hours to 20 mg and in 2 days to normal. The cerebrospinal fluid, after test doses of 1 gram, contained 1.82–4.18 mg/100 ml.

Vitamin C is eliminated in urine, faeces and sweat. The urinary excretion depends on the C-intake and -supply of the body, and rises and falls with the level in plasma. There is no sharply defined renal threshold value, the value varying between 1.1 and 1.3 mg

per 100 ml plasma, the zone in which the elimination curve starts to rise. In severe C-deficiency the threshold value falls to 0.85 mg. – With an additional intake of 50–100 mg the plasma level after 12 days (equilibrium) reaches 0.97 mg (summer) or 0.89 mg (winter), the corresponding values for 24-hour urinary excretion being 26.7 mg (total vitamin C; reduced vitamin C, 25.6 mg) and 31.4 mg (reduced vitamin C, 24.4 mg).

The renal elimination is increased by many substances, e.g. by foodstuffs such as cabbage and oats, by drugs such as fish oils, salicylates, atropine, acetylsalicylic acid, barbiturates, antipyrine, adrenaline, chloroform, paraldehyde, stilboestrol, oestradiol, sulphonamides, as well the normal anaesthetics. Insulin and sodium bicarbonate lower the elimination.

The excretion in faeces is fairly constant at ca. 5 mg per day, even large variations in the intake having no effect. It can, however, be markedly increased by intestinal disturbances.

A loss in sweat during severe bodily exertion amounting to 2 mg per hour has been reported but it has not been confirmed as the general case.

Vitamin C is synthesized in all the higher plants and in most animal organisms with the exception of man and guinea pigs. It is indispensable for the building up of intracellular substances such as collagen, probably also for intracellular oxidation-reduction processes and for the metabolism of aromatic amino-acids.

The daily requirement of vitamin C under normal conditions is estimated at 50 mg. According to more recent researches (SCHEUNERT, *Z. Vitamin-, Hormon- u. Fermentforsch.*, **20** (4), 374, 1949) it is even higher, with a minimum of 75 mg and an optimum of 125 mg. Extensive observations have shown that administration of vitamin C at this level definitely increases the resistance to infectious disease. C-Activity is promoted by vitamin P and vice versa. This synergistic effect amounts to up to 56% and is particularly evident with submaximal doses of cryst. vitamin C, the biological effect of which is markedly increased by simultaneous P-administration (CRAMPTON and LLOYD, *J. Nutr.*, **41**, 487, 1950).

As indispensable factor in cell metabolism, vitamin C influences all the bodily tissues, particularly the bones and teeth. Deficiency results in characteristic changes in the gingiva, in reduced capillary resistance, in diminished resistance to infections, in slower healing of wounds and fractures, in fatigability and general lassitude, in anaemia; in the growing organism it causes defects in bones and teeth.

Therapeutic application

In all C-hypovitaminoses, scurvy, MÖLLER-BARLOW disease and related conditions; increased C-requirement in infectious diseases, pregnancy, lactation, infants on artificial nourishment. Experimentally, in haemorrhagic diatheses together with vitamin P.

Vitamin P¹

The vitamin factor which, independently of vitamin C, is necessary for the maintenance of normal capillary resistance is known as vitamin P or citrin. The latter name has its origin in the observation that lemon juice contained other factors, apart from vitamin C, which had a favourable effect on capillary resistance.

Strong vitamin-P activity is shown particularly by all citrus fruits and black currants. A series of compounds with P-activity is now known: flavones (e.g. phenylchromone), flavanones (e.g. eriodictyol, hesperidin, and hesperitin), flavanols (e.g. 2-phenyl-3-hydroxy-1:4-benzopyrone and rutin), catechin, epicatechin, phloretin.

Unit. None.

Methods of test and assay. None satisfactory.

¹) See also *Vitam. and. Horm.*, **7**, 1949.

²) In sharp contrast to experimental animals. Cf. LEVITAN, A. B., *Amer. J. med. Sci.*, **221**, 185, 1951.

³) SOKOLOFF et al., *J. clin. Invest.*, **30**, 395, 1951.

Vitamin B₁ (thiamine, aneurine)

Thiamine occurs in nature as the free compound (in plants), as the pyrophosphate (co-carboxylase) or as the pyrophosphate-magnesium-protein complex (the latter two in animals). It is soluble in water and aqueous alcohol, insoluble in fat solvents, stable to heat in strongly acid solutions, unstable in neutral and alkaline solutions. It is stable to atmospheric oxygen but rapidly decomposed by oxidizing agents, unstable to ultraviolet light. Optically inactive, it possesses strong absorption maxima at 2330 and 2670 Å.

The thiamine molecule consists of a pyrimidine and a thiazole component:

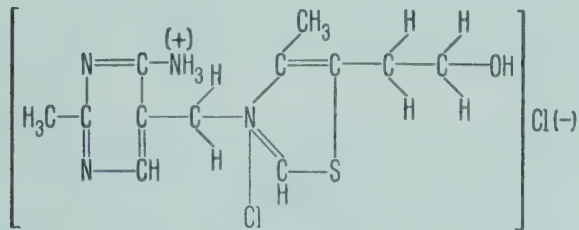
Thiamine hydrochloride, C₁₂H₁₈ON₄SCl₂

Mol. wt. 337.28

Colourless monoclinic needles

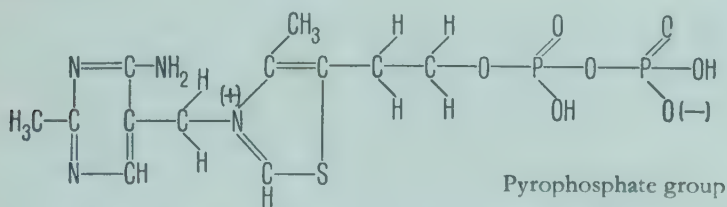
Nutty odour

M. p. 248–250 °C



Pyrimidine component Thiazole component
(after U.S. Pharmacopeia XV, 1955)

Co-carboxylase



(after U.S. Pharmacopeia XV, 1955, and LOHMANN)

Units

1 international unit (I.U.) = 0.003 milligram thiamine hydrochloride = 1 British unit = 1 U.S. Pharmacopeia unit.

Methods of test and assay

Thiochrome method: Thiamine is oxidized to thiochrome by means of potassium ferricyanide in alkaline solution and the thiochrome determined by its intense blue fluorescence in ultraviolet light (official method in USA for pharmaceuticals and foodstuffs).

Biologically (rat protection test, rat growth test, yeast fermentation test).

Microchemically by the very delicate method of WESTENBRINK, permitting the determination of thiamine and co-carboxylase in their mixtures, with a sensitivity of 0.0005 µg thiamine and 0.00005 µg co-carboxylase (WESTENBRINK, H. G. K., *Enzymologia*

Physiology and function

Unexplained, particularly in man. Recent studies by French workers indicate that the P-activity (increase of capillary resistance) is a secondary effect exercised via an inhibition of the oxidation of acetylcholine.

Therapeutic application

As supplement in scurvy and similar diseases, in haemorrhagic diatheses (no effect in thrombopenic purpura or in retinal haemorrhage in diabetes²), in haemorrhagic nephritis, in pneumonia, in gestosis, for pre-operative diminution of capillary fragility, for prophylaxis of apoplexy due to increased blood pressure, for control of the diminution of capillary resistance exercised by dicumarol, preferably in the form of rutin. Erythema due to X-rays may be greatly reduced or even completely prevented by administration of 300–600 mg of vitamin P from citrus fruits³.

8, 97, 1940). Using alkali-washed yeast as adsorbent and apoenzyme, this method permits the determination of the co-carboxylase content of 0.01 ml of blood (WESTENBRINK et al., *Z. Vitaminforsch.*, **13**, 218, 1943; PARVÉ, E. P. S., *Thesis*, Scheltema and Holkema, Amsterdam, 1945).

Occurrence (values are in I.U. per 100 g weight fresh)

Yeast 2000–30,000, wheat germ 600–1250 (wholemeal bread, wheat or rye 75–150), spinach 175–400, pork 280–400, widely distributed in nature.

Physiology and function

Thiamine is synthesized by plants and a number of microorganisms. It is possible that it is formed by the intestinal flora in the animal organism but the latter is mainly dependent for its supply on foods of vegetable origin (free thiamine) or of animal origin (co-carboxylase). – Thiamine itself is rapidly absorbed in the intestine and is phosphorylated by all types of nucleate cell, particularly in the liver, and is dephosphorylated in the kidneys and excreted as free vitamin. A large part is also decomposed in the body and appears in the urine as organic sulphur compounds. The organism is incapable of storing vitamin B₁; three hours after ingestion of a large dose the greater part is already eliminated. The total quantity excreted is roughly proportional to the quantity of urine: severe diuresis thus results in a considerable loss of B₁. Small quantities are also eliminated in sweat.

The blood level amounts to ca. 6–12 µg/100 ml as co-carboxylase in the corpuscles and ca. 1 µg as free vitamin in plasma. The content in the cerebrospinal fluid corresponds to that in plasma. The co-carboxylase content of the leucocytes is ca. 10 times greater than that of the erythrocytes. The blood level is markedly lower in alcoholic and alimentary neuritis, as well as in scurvy.

The daily requirement rises and falls with the intake of calories. According to COWGILL, G. R., *Vitamin B Requirements of Man*, New Haven, 1934, the minimum requirement in health is given in mg of B₁ as $4.26 \times 10^{-6} \times \text{body weight in kilograms} \times \text{daily calorie intake}$. The optimal supply is about 50% higher. In children the requirement in proportion to body weight is somewhat greater (according to HOLT et al., *J. Nutr.*, **37**, 53, 1949, the minimal requirement of 4–11 months infants on artificial nourishment is 0.14–0.20 mg/day).

As pyrophosphate, thiamine forms the prosthetic group of various enzymes with specific action on α-keto-fatty acids, particularly pyruvic acid. Since pyruvic acid occupies a key position in carbohydrate metabolism as intermediate and end-product of certain anaerobic processes and as starting point of decarboxylation and oxidation, it follows that thiamine is an important regulator of carbohydrate metabolism, together with riboflavin, pyridoxine and nicotinic acid, constituents of other co-enzymes participating in carbohydrate metabolism. In B₁-deficiency the pyruvic acid value of the blood rises sharply, often also the lactic acid value. Administration of B₁ lowers these values rapidly. Cf. pyruvic acid in blood, page 322.

It is not yet certain whether the effect of thiamine on the activity of the nervous system is a primary effect (synergist of acetylcholine) or the result of its capacity to regulate carbohydrate metabolism, or both (see VON MURALT, A., *Vitam. and Horm.*, 5, 93, 1947)

Thiamine has no effect on protein metabolism. – The B₁-economizing effect of fats is explained by the fact that a greater part of the calorie demand of the body is met by fat metabolism, resulting in a reduced carbohydrate metabolism and thereby in a reduced need for thiamine.

The thiamine enzymes are mostly protein-magnesium-carboxylase complexes in which the magnesium can be replaced by other bivalent metals. These enzymes are blocked by heavy metals and certain organic compounds such as pyruvic ester. Acetyl iodide, mustard gas and arsenites also block the pyruvic acid-oxidase enzyme system, a discovery which finally led to the synthesis of BAL (2:3-dimercaptopropanol), the antidote to certain war gases and heavy-metal poisons.

Therapeutic application

B₁-Deficiency tests on man give rise to the following symptoms: loss of appetite, nausea, general lassitude; hypomotility and hypo-

tonia of stomach and intestines, hypochlorhydria and achlorhydria, obstipation; loss of weight (interrupted growth in children); tachycardia and reduced T-amplitudes in the electrocardiogram; disturbances in water balance (hydrolability, tendency to oedemas and to sudden loss of water); neurological symptoms, particularly in the legs: weakness of the calf muscles, muscle cramps, fatigability, hyperaesthesia and anaesthesia; in severe deficiency, polyneuritis, beri-beri.

These symptoms may be most effectively and rapidly eliminated by administration of the whole B complex (combination preparations, yeast, liver or liver extracts) since a B₁-deficiency alone seldom or never occurs. Cases are known in which an exclusive high-dosage B₁-therapy has led to symptoms of a marked B₂- and nicotinic acid deficiency (disturbance of the latent deficiency balance, see also Folic acid, page 219).

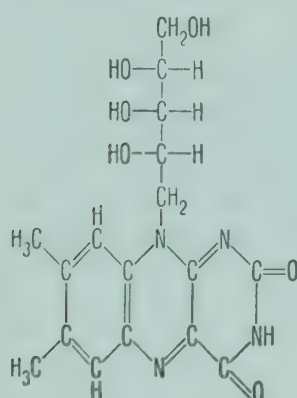
In cases of neuritis high doses of vitamin B₁ should be tried (likewise in conjunction with the whole B complex): dietary deficiencies, alcoholism, gastro-intestinal troubles, disturbances of the liver, pregnancy, diabetes; successful results are only to be expected, however, when the neuritis is due to B₁-deficiency. B₁ can be tried as protective therapy in lead neuritis. In delirium tremens nicotinic acid has mostly been found to be more effective.

Vitamin B₂ (riboflavin, lactoflavin)

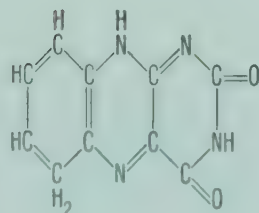
Vitamin B₂ occurs in nature either in the free form or as co-enzyme in protein complexes. The pure vitamin is only sparingly soluble in water and alcohols and insoluble in fat solvents; it is stable to heat when dry or in acid solution, stable to atmospheric oxygen, unstable in alkaline solution and to light. Solutions exhibit an intense yellowish-green fluorescence. The name riboflavin is derived from its colour and from the ribose component of the molecule. Structurally it is a derivative of isoalloxazine.

Vitamin B₂, C₁₇H₂₀O₆N₄

Mol. wt. 376.36
Orange-yellow crystals, blackening at 240°C
Bitter taste
M. p. (decomp.) 275–282°C



Isoalloxazine



Unit

No international unit; by weight.

Methods of test and assay

Microbiologically by means of *Lactobacillus helveticus* (casei) and others, rat growth test, fluorometrically.

Occurrence (values are in mg per 100 g weight fresh)

Yeast 2–4; liver of various animals 2–3.5; meat extract 1–2.5; kidneys 1–2; human milk 0.06 mg/100 ml (Sos, J., *Z. Vitamin-, Hormon- u. Fermentforsch.*, 1, 369, 1948); widely distributed in all leaf vegetables, in flesh of warm-blooded animals and fish.

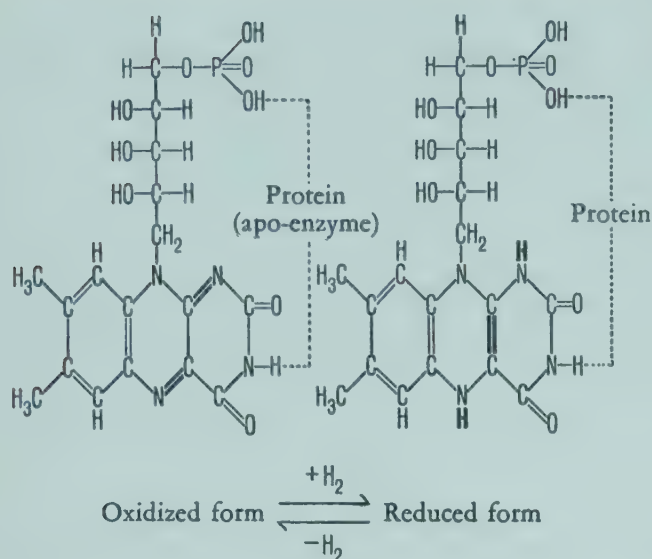
Physiology and function

In man it is difficult to bring about a B₂-hypovitaminosis or -avitaminosis through a diet deficient in this vitamin. Since the B₂ content of the faeces often exceeds that of the diet it is reasonable to assume that the vitamin is synthesized by the intestinal flora. In infants a daily intake of 0.4 mg B₂ suffices to maintain the blood level and urinary excretion at the lower limit of the minimum (SNYDERMAN et al., *J. Nutr.*, 39, 219, 1949). The urinary excretion of adults amounts to 0.543–0.913 (mean 0.678) mg/day, the excretion in faeces to 0.183–0.361 (mean 0.246) mg/day (after ROBINSON, F. A., *The Vitamin B Complex*, New York, 1951, pages 77 and 78). Riboflavin is phosphorylated in the intestinal wall, and stored in the liver, spleen and kidneys. These depots are as far as possible maintained and in even the most severe deficiency suffer a reduction of only about 30%. B₁-Deficiency and increased protein intake result in increased storage and lowered excretion of vitamin B₂, and vice versa. Riboflavin is excreted in urine as uroflavin, a pigment which is almost identical with it as regards composition, properties and vitamin activity. The daily elimination on a normal diet amounts to ca. 12% of the intake but bears no hard and fast relationship to the latter. – Small amounts are also eliminated in sweat.

The riboflavin content of the blood is ca. 280–300 µg/100 g (whole blood); 3.5–4.0 µg/100 g (serum); 25 µg/100 g (erythrocytes); 250–260 µg/100 g (leucocytes), mainly as dinucleotide.

As phosphoric ester (mononucleotide) riboflavin forms the prosthetic group of WARBURG's yellow respiratory enzyme. This enzyme was the first to be discovered of a whole series of oxi-

Bibliography: The data in the section "Vitamins" have been based on the following literature, in addition to that cited in the text: ABDERHALDEN, E., *Physiologische Chemie*, Basle, 1948; BICKNELL and PRESCOTT, *The Vitamins in Medicine*, London, 1946; CLARK, G. W., *A Vitamin Digest*, Springfield, 1953; GYÖRGY, P., et al., *Vitamin Methods*, New York, 1950–51; CONN et al., *Current Therapy*, Philadelphia, 1955; HOTZEL, A., *Vitamine und Vitaminpräparate*, Aulendorf, 1949; SUNDERMAN and BOERNER, *Normal Values in Clinical Medicine*, Philadelphia, 1950; GROSSE-BROCKHOFF, *Pathologische Physiologie*, Berlin, 1950; LEHNARTZ, E., *Chemische Physiologie*, Berlin, 1948; KARRER, P., *Lehrbuch der organischen Chemie*, Stuttgart, 1950; ROBINSON, F. A., *The Vitamin B Complex*, New York, 1951; *Vitam. and Horm.*, 1949–52; *Z. Vitaminforsch.*, 1948–53; *J. Nutr.*, 1949–53; *Ann. Rev. Biochem.*, 1950–53.



Riboflavin as coenzyme (mononucleotide) of WARBURG's yellow respiratory enzyme (after KUHN).

dation enzymes (oxidases) differing from WARBURG's enzyme in the structure of the prosthetic group (dinucleotides) and exhibiting much greater activity (up to 1000 times greater). The prosthetic group of these enzymes is an adenine dinucleotide to which the riboflavin molecule is linked both at position 5 in the ribose nucleus and at C₆ of the side chain via a pyrophosphate group. The effect of all these respiratory enzymes resembles that of WARBURG's enzyme and consists in a reversible oxidizability and

reducibility (see formula), a so-called redox system. Among the yellow oxidases are D-amino-acid oxidase, xanthine oxidase (aldehyde oxidase, SCHARDINGER's reductase), the diaphorases and cytochrome C reductase. The enzyme systems of riboflavin are closely related to others in which thiamine, nicotinic acid and pyridoxine act as components of coenzymes.

In the organism riboflavin occurs not only as coenzyme but also in the free form in the retina, cornea and lens; together with vitamin A and nicotinamide it appears to play an important role in the visual processes (cf. Vitamin A, page 209).

Diagnosis and therapy of B₂-deficiency

In man there is no absolutely specific symptom of riboflavin deficiency. Of diagnostic value are seborrhoeic lesions of the nasolabial folds, eyelids and ears; mouth-corner rhagades; dry, itching dermatitis of the anus, vulva and scrotum, burning sensation on the tongue and feet, glossitis, retrobulbar neuritis followed by partial optical atrophy, anaesthesia and paraesthesia of feet and legs as well as STANNUS's cerebellar syndrome (muscular asthenia and hypotonia, ataxia, clonic contractions, augmented reflexes, dysmetria, nystagmus, dysdiadokinesia, vertigo, tremors, pendular knee-jerk reflexes). Vascularization of the cornea and capillary dilatation of the skin are non-specific symptoms which occur in other vitamin deficiencies as well as in deficiency of certain essential amino-acids.

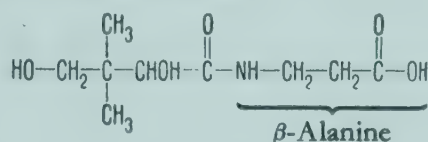
The diagnosis is confirmed by the therapy: if after several days treatment with a daily dose of 10 mg there is no improvement, it may be assumed there is no riboflavin deficiency.

Pantothenic acid

This vitamin occurs naturally as the free acid, but preparations usually consist of the calcium salt. It is soluble in water, insoluble in benzene and chloroform, unstable to acids, bases and heat. The calcium salt is water-soluble and more stable to heat.

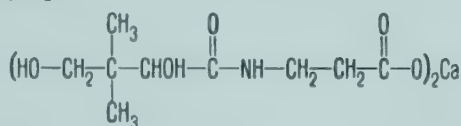
Pantothenic acid, C₉H₁₇O₅N

Mol. wt. 219.23
Yellow viscous oil



Calcium pantothenate, (C₉H₁₆O₅N)₂Ca

Mol. wt. 476.53
White crystals
Sweet taste, odourless



Unit

No international unit; by weight.

Methods of test and assay

Microbiologically by means of *Lactobacillus helveticus* (casei) or *L. arabinosus* (HOAG et al., *Ind. Eng. Chem. Anal. Ed.*, **17**, 60, 1945); growth test on chicks or yeast.

Occurrence (values are in mg per 100 g weight fresh)

Yeast 14–35; liver 7–8; dried beans, mushrooms, roasted peanuts 1–2.5; human milk 0.2 mg/100 ml (SCHMIDT, V., *Z. Vitaminforsch.*, **8**, 21, 1950); widely distributed in all plant and animal tissues.

Physiology and function

Pantothenic acid can be synthesized by plants, by some micro-organisms and by rodents (very probably by the intestinal flora).

Deficiency of pantothenic acid results in the following symptoms. *Rats*: greying hair in young animals; adrenal haemorrhages, increased disposition to stress¹; vascularization of the cornea characterized by numerous large capillaries with prominent anastomosis²; atrophy of the intestinal mucosa and duodenal ulcers (the latter in 60% of experimental animals)³. *Dogs*: hypoglycaemia and gastrointestinal disturbances; fatty infiltration of the liver, convulsions. *Chicks*: dermatitis. *Mice*: bone changes⁴. Only little is known of the biochemistry of pantothenic acid. It is a component of the coenzyme A necessary for all acetylation processes (preparation from pig's liver: HIGGINS et al., *Fed. Proc.*, **10**, 384, 1951). Pantothenic acid-deficient rats treated with sulphanilamide excreted much less acetylsulphanilamide than the control animals⁵; the capacity for acetylation of *p*-aminobenzoic acid is also markedly reduced (this is also the case, but to a much smaller extent, in B₂-deficiency and, to an even smaller extent, in B₁-deficiency)⁶.

The urinary excretion amounts to 2.5–5 mg/24 hours.

For a bibliographical review see BRISKAS, S., *Z. Vitaminforsch.*, **23**, 63, 1951.

Therapeutic application

Since the adrenocortical tissue is particularly sensitive to pantothenic acid deficiency it is worth trying this vitamin as adjuvant in adrenocortical insufficiency. In ADDISON's disease, diabetes or cirrhosis of the liver, pantothenic acid has no effect on the blood sugar or blood phosphate level⁷.

¹) DUMM et al., *Proc. Soc. exp. Biol.*, **71**, 368, 1949. ²) BOWLES et al., *J. Nutr.*, **37**, 9, 1949. ³) BERG et al., *Proc. Soc. exp. Biol.*, **71**, 374, 1949. ⁴) LEVY, B. M., *J. Amer. dent. Ass.*, **38**, 215, 1949. ⁵) SHILS et al., *J. Nutr.*, **37**, 227, 1949. ⁶) RIGGS and HEGSTED, *J. biol. Chem.*, **178**, 669, 1949. ⁷) GERSHBERG et al., *J. Nutr.*, **39**, 107, 1949.

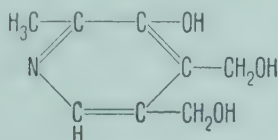
Bibliography: The data in the section "Vitamins" have been based on the following literature, in addition to that cited in the text: ABDERHALDEN, E., *Physiologische Chemie*, Basle, 1948; BICKNELL and PRESCOTT, *The Vitamins in Medicine*, London, 1946; CLARK, G. W., *A Vitamin Digest*, Springfield, 1953; GÖRGY, P., et al., *Vitamin Methods*, New York 1950–51; CONN et al., *Current Therapy*, Philadelphia, 1955; HOTZEL, A., *Vitamine und Vitaminpräparate*, Aulendorf, 1949; SUNDERMAN and BOERNER, *Normal Values in Clinical Medicine*, Philadelphia, 1950; GROSSE-BROCKHOFF, *Pathologische Physiologie*, Berlin, 1950; LEHNARTZ, E., *Chemische Physiologie*, Berlin, 1948; KARRER, P., *Lehrbuch der organischen Chemie*, Stuttgart, 1950; ROBINSON, F. A., *The Vitamin B Complex*, New York, 1951; *Vitam. and Horm.*, 1949–52; *Z. Vitaminforsch.*, 1948–53; *J. Nutr.*, 1949–53; *Ann. Rev. Biochem.*, 1950–53.

Vitamin B₆

Vitamin B₆ occurs in nature in at least three forms, as pyridoxine, pyridoxal and pyridoxamine, of which for a long time only the first was known. Pyridoxine is soluble in water, alcohol and acetone, sparingly soluble in organic solvents, stable to heat and concentrated acids and alkalis but unstable to light.

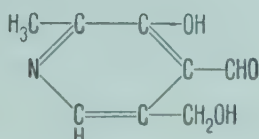
Pyridoxine (adermin), C₈H₁₂O₃N

Mol. wt. 170.19



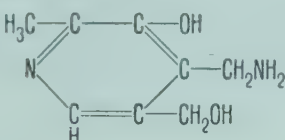
Pyridoxal, C₈H₉O₃N

Mol. wt. 167.16

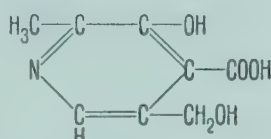


Pyridoxamine, C₈H₁₂O₂N

Mol. wt. 168.19



4-Pyridoxic acid



Units

No international unit; by weight.

Methods of test and assay

Microbiologically by means of *Lactobacillus helveticus* (casei), *Streptococcus faecalis* and *S. carlsbergensis* for pyridoxine, pyridoxal and pyridoxamine (SNELL, E. E., *J. biol. Chem.*, **157**, 491, 1945; RABINOWITZ and SNELL, *ibid.*, **169**, 631, 1947).

Occurrence (values are in mg per 100 g weight fresh)

Dried yeast 3.6; cereal germ 0.6–1.7; potatoes 0.2–0.3; widely distributed in small concentrations in all animal and plant tissues.

Physiology and function

In animal tissues the vitamin occurs mainly as pyridoxal and pyridoxamine; in plant tissues pyridoxine is also found, although mostly in much smaller quantities¹. In human urine only pyridoxal and 4-pyridoxic acid occur, the latter as degradation product without vitamin activity; this is also the case when pyridoxamine or pyridoxine is administered. Exogenous pyridoxal raises the urinary pyridoxic acid level much more than pyridoxamine or pyridoxine².

Symptoms of B₆-deficiency. *Rats*: severe dermatitis (rat pellagra), amenable to treatment by essential unsaturated fatty acids ("vitamin F"). *Syrian hamsters*: muscular weakness, atrophy of lymph glands and adipose tissues, increased excretion of xanthurenic acid in urine. The appearance of deficiency symptoms can be delayed by administration of maize oil, but not prevented. Once established a B₆-deficiency is not amenable to this treatment³. *Rhesus monkeys*: most frequent and dominating symptom: sclerosis of, *inter alia*, arteries, pancreas, kidneys and spleen⁴. *In man* after a 3-week deficiency: increased excretion of xanthurenic acid after experimental doses of tryptophan (normalized in one week by 15 mg pyridoxine hydrochloride)⁵.

Vitamin-B₆ deficiency develops slowly, without distinctive clinical symptoms. The normal average blood level of 11 µg/100 ml whole blood (range 5–25 µg/100 ml) falls within 2–4 weeks after the start of a B₆-deficient diet to 2–3 µg/100 ml (expressed as pyridoxine hydrochloride) and remains at this level as long as the diet continues⁶.

Pyridoxal is a coenzyme of various decarboxylases and transaminases and appears to be important for amino-acid and fat metabolism. For example, pyridoxal phosphate is the coenzyme of kynureninase in the liver cells which breaks down kynurenin into anthranilic acid and alanine⁷. It is possible that the conversion of tryptophan into nicotinamide is due to the action of a similar B₆ enzyme (3-hydroxykynurenin → 3-hydroxyanthranilic acid). According to UMBREIT and GUNSALUS⁸ codecarboxylase is pyridoxal 5-phosphate (confirmed by⁹).

Therapeutic application

Supporting therapy in pellagra (with nicotinamide, q.v.). Experimentally in muscle spasms and chorea. In hyperemesis gravidarum for the normalization of the lowered urea level in blood (40 mg over 3 days)¹⁰.

¹) RABINOWITZ and SNELL, *J. biol. Chem.*, **176**, 1157, 1948. ²) RABINOWITZ and SNELL, *Proc. Soc. exp. Biol.*, **70**, 235, 1949. ³) SHWARTZMAN and STRAUSS, *J. Nutr.*, **38**, 131, 1949. ⁴) RINCHART and GREENBERG, *Amer. J. Path.*, **25**, 481, 1949. ⁵) GREENBERG et al., *Arch. Biochem.*, **21**, 237, 1949. ⁶) GREENBERG and RINEHART, *Proc. Soc. exp. Biol.*, **70**, 20, 1949. ⁷) BRAUNSHTEIN et al., *Biokhimiya*, **14**, 163, 1949, and *Chem. Abstr.*, **43**, 6264, 1949. ⁸) UMBREIT and GUNSALUS, *J. biol. Chem.*, **179**, 279, 1949. ⁹) SLOANE-STANLEY, *Biochem. J.*, **44**, 567, 1949. ¹⁰) MCGANITY et al., *J. biol. Chem.*, **178**, 511, 1949.

Nicotinic acid (niacin)

Nicotinic acid occurs in nature mainly as the amide, nicotinamide, and only to a small extent as the free acid. It is soluble in water and alcohol, insoluble in fat solvents, stable to heat and oxidation. Nicotinic acid is a derivative of pyridine.

Unit

No international unit; by weight.

Methods of test and assay

Microbiologically (*Lactobacillus arabinosus* for nicotinic acid + nicotinamide, *Leuconostoc mesenteroides* for nicotinic acid alone), black-tongue curative test on dogs, growth test on chicks. Colorimetrically.

Occurrence (values are in mg per 100 g weight fresh)

Meat extract, yeast 30–100; rice bran 20–140; liver 10–20; widely distributed in all animal and vegetable foods except pure fats. During fermentation the content of nicotinic acid in tobacco leaf rises to 0.4%¹.

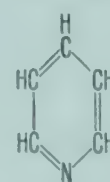
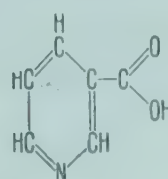
Nicotinic acid, C₆H₅O₂N

Mol. wt. 123.11

M. p. 234–237 °C

White crystals, odourless, acid taste

(Pyridine)



Nicotinamide, C₆H₆ON₂

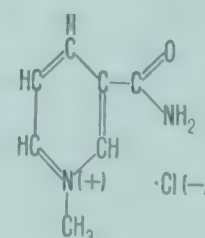
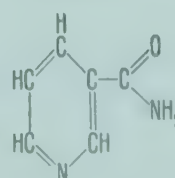
Mol. wt. 122.12

M. p. 128–131 °C

White crystals, odourless, bitter taste

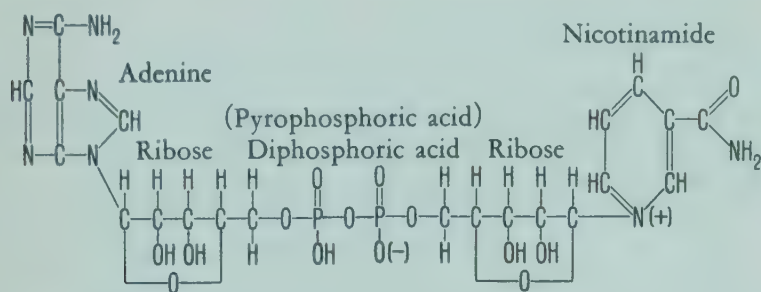
N¹-Methylnicotinamide

(Nicotinamide methochloride)



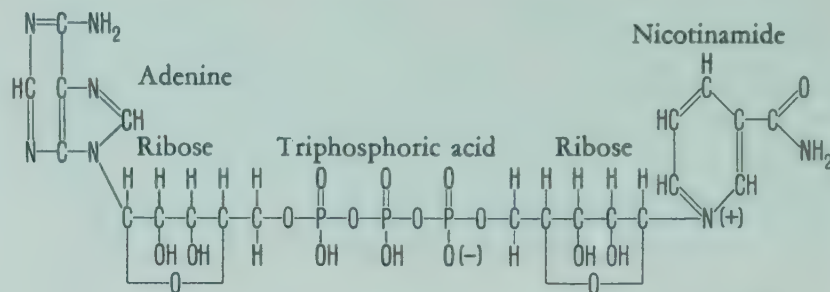
Biotin

Codehydrase I, DPN (diphosphopyridine nucleotide), coenzyme I, cozymase



(after ROBINSON, F. A., *The Vitamin B Complex*, New York, 1951)

Codehydrase II, TPN (triphosphopyridine nucleotide), coenzyme II



(after ROBINSON, F. A., *The Vitamin B Complex*, New York, 1951)

Physiology and function

Under normal conditions the blood level amounts to 0.30–0.83 mg/100 ml (whole blood), of which the greater part is in the blood corpuscles as codehydrase I. – Nicotinic acid is present in all the tissues and is stored by the liver.

Nicotinic acid can be synthesized from tryptophan by all mammals and most bacteria². The course of the biosynthesis is as follows³:

tryptophan → kynurenin → 3-hydroxykynurenin → 3-hydroxyanthranilic acid → quinolinic acid → nicotinic acid

In man intravenous administration of tryptophan does not raise the excretion of nicotinic acid degradation products as much as oral administration, indicating that the body's own synthesis is supplemented by that of the intestinal flora. – In order for it to fulfil its function in protein synthesis tryptophan must be accompanied by other essential amino-acids, a condition which is not necessary for its role as precursor of nicotinic acid⁴.

Nicotinamide is excreted in urine 80% as N¹-methylnicotinamide, as N¹-methyl-2-pyridone-5-carboxylamide and as acid-hydrolyzable derivatives of nicotinic acid⁵. The total per day amounts to 9.5–44 mg. In the latter 5 months of pregnancy excretion of nicotinamide increases⁶. – Trigonelline (the N-methylbetaine of nicotinic acid) is not a degradation product of nicotinic acid, as formerly assumed: the amount excreted in urine is not increased by exogenous nicotinic acid but is increased after the consumption of foods containing trigonelline, such as vegetables and particularly coffee.

As nicotinamide, nicotinic acid is a component of the coenzymes of dehydrases I and II (see structural formulae above) which

participate on a variety of substrates in carbohydrate and protein metabolism. In these coenzymes nicotinamide can be replaced without loss of function in the system by a number of other pyridine derivatives, e.g. by nicotinic acid N-diethylamide (nikethamide, coramine), quinolinic acid, 2:6-dimethylpyridine-3:5-dicarboxylic acid, pyrazine-mono- and -2:3-di-carboxylic acids.

Pharmacology

Nicotinic acid, *but not nicotinamide*, in large doses causes a marked vasodilatation, particularly in the vessels of the upper half of the body. Subjective secondary symptoms in parenteral application are sensation of warmth, "pins and needles" and pruritus, together with slight vertigo, pressure sensation in the head or headache, occasionally nausea, vomiting and transient abdominal pains.

Therapeutic application

Nicotinic acid. In peripheral circulatory disturbances, angina pectoris, asthma.

Nicotinamide. In pellagra together with vitamin B₁, vitamin C and liver extract; in nervous disturbances due to X-rays (+ total B complex, also prophylactically effective, particularly in undernourished and weakened patients); alimentary or toxic dermatosis (particularly in diabetes); glossitis (see also Riboflavin); stomatitis of indeterminate origin; in liver diseases (porphyria); in certain psychoses (psychoses resembling senile, arteriosclerotic, toxic or exhaustion psychoses occurring suddenly or after a short prodromal stage in patients who are old, undernourished or weakened by illness); occasionally effective in delirium tremens.

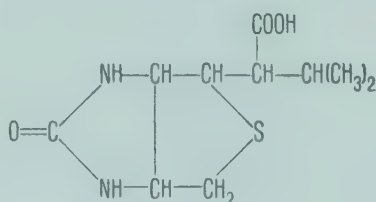
¹) FRANKENBURG and GOTTSCHO, *Arch. Biochem.*, **21**, 247, 1949. ²) HENDERSON and HANKES, *Proc. Soc. exp. Biol.*, **70**, 26, 1949, HUNDLEY, J. M., *ibid.*, **70**, 592, 1949, and SNYDERMAN et al., *ibid.*, **70**, 569, 1949. ³) HEIDELBERGER et al., *J. biol. Chem.*, **176**, 1461, 1949; **179**, 143 and 151, 1949. ⁴) GEIGER et al., *Arch. Biochem.*, **23**, 315, 1949. ⁵) HOLMAN and LANGE, *Biochem. J.*, **45**, 559, 1949. ⁶) FRAZIER et al., *J. Nutr.*, **37**, 393, 1949.

Biotin (vitamin H)

Biotin occurs naturally in two forms, α- and β-biotin. Both forms are soluble in water and alcohol, sparingly soluble in ether and chloroform, stable to heat, and inactivated by acids, alkalis, rancid fats and choline.

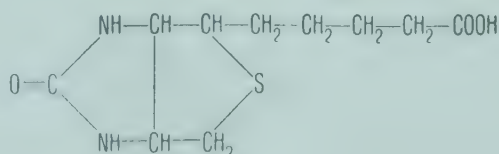
α-Biotin (KöGL), C₁₀H₁₆O₃N₂S

Mol. wt. 244.30
M. p. 220 °C



β-Biotin (DU VIGNEAUD), C₁₀H₁₆O₃N₂S

Mol. wt. 244.30
White crystals
M. p. 232–233 °C



Methods of test and assay

Microbiologically by means of *Lactobacillus helveticus* (casei) or *L. arabinosus*. No chemical or physical methods yet developed.

Occurrence (values are in mg per 100 g weight fresh)

Yeast (*Torula utilis*) 0.13; roasted groundnuts and chocolate 0.032–0.034; dried peas and mushrooms 0.016–0.018; widely distributed in small concentrations in all animal and plant tissues.

Physiology and function

Nothing definite is known of the biochemistry of biotin. It is synthesized by the intestinal flora and the excretion in faeces is always greater than the oral intake¹. The biotin synthesized by the intestinal flora, however, undergoes no (or only very slight) resorption since the urinary excretion is proportional to the biotin intake. On a normal diet the urinary excretion amounts to 27.5 to 35.6 μg/24 hours.

Raw egg albumin contains a protein, avidin, which combines in the body with biotin, thus rendering it unavailable (egg-white injury). There is reason to believe that biotin is a vitamin indispensable to the organism, although diseases of biotin deficiency are extremely rare. In deficiency experiments the following

Para-aminobenzoic Acid – Folic Acid Group

symptoms have been observed²: mild dermatitis commencing after 4 weeks and developing by the 7th week into desquamative patches on the hands, arms and legs; during the 7th and 8th weeks the skin takes on a marked greyish tinge; tongue white, papilla atrophied; after the 5th week there appear in addition muscular pains, hyperaesthesia, localized paraesthesia, loss of appetite, nausea and psychic depression; fall in erythrocytes, haematocrit value and haemoglobin in spite of sufficient iron; increase of bile pigments and cholesterol in blood. Treatment with 75–300 µg biotin per day resulted in disappearance of the symptoms in 3–5 days.

The biotin content of tumour tissues is abnormally high. An experimental therapy in man based on this fact (creation of a biotin deficiency by means of a diet rich in raw egg albumin) was, however, unsuccessful.

Therapeutic application

Where biotin deficiency is suspected: in status seborrhoicus in infants, acne, furunculosis.

¹) OPPEL, T. W., *Amer. J. med. Sci.*, **204**, 886, 1942.

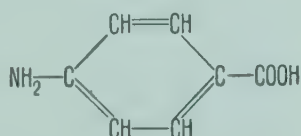
²) SYDENSTRIKER et al., *Science*, **95**, 176, 1942.

Para-aminobenzoic acid

This compound occurs in nature in the free or acetylated form or in combination with peptides. It is soluble in alcohol and in boiling water, stable in acid and alkaline solutions, unstable in the presence of oxidizing agents.

p-Aminobenzoic acid, C₇H₇O₂N

Mol. wt. 137.13
Colourless crystals
M. p. 186–187°C



Unit

No international unit; by weight.

Methods of test and assay

Microbiologically by means of *Clostridium acetobutylicum*¹ or *Neurospora crassa*².

Occurrence (values are in mg per 100 g weight fresh)

Yeast 0.4–10.0; beef liver 0.25; mushrooms 0.13; wheat germ 0.1; spinach 0.06; oat flakes 0.033; corn meal 0.03; egg powder (whole egg) 0.02–0.036; calf liver 0.02; milk 0.015 per 100 ml.

Physiology and function

The urinary excretion amounts to 0.131–0.198 mg/day, mean 0.148; in faeces 0.183–0.361 mg/day, mean 0.246.

The reciprocal blocking effect of *p*-aminobenzoic acid and sulphonamides justifies the assumption that the former is a component of a coenzyme which is important at least for micro-organisms.

In rats *p*-aminobenzoic acid is indispensable for normal pigmentation, in chickens for normal growth. Nothing is known of its function in man.

Therapeutic application

In high concentrations *p*-aminobenzoic acid has a bacteriostatic effect on Rickettsia which is, however, far exceeded by modern antibiotics. – *p*-Aminobenzoic acid acts synergistically with cortisone in rheumatism, so that the cortisone dosage can be considerably reduced³. – Patients who are administered large amounts of *p*-aminobenzoic acid excrete abnormally large amounts of glucuronic acid, to such an extent that the fermentation test for glucose is suppressed⁴.

¹) LAMPEN and PETERSON, *J. biol. Chem.*, **153**, 193, 1944.

²) THOMPSON et al., *J. biol. Chem.*, **148**, 281, 1943.

³) BARRIT and STUMPE, *Amer. J. med. Sci.*, **22**, 3, 1951.

⁴) ZARAFONETIS and CHANDLER, *J. Lab. clin. Med.*, **37**, 425, 1951.

Folic acid group

The name folic acid was given by MICHELL et al.¹ in 1941 to a vitamin-like substance which he had isolated from spinach leaves. The structure of this compound has remained unknown and the name folic acid is now generally used to designate pteroylglutamic acid (PGA), a vitamin with activity similar to that of MITCHELL's substance. A whole series of compounds with activity similar to folic acid has since been discovered. The relations between these compounds have not yet been fully elucidated but it is almost certain that they are vitamin precursors and that only one or two members of the group can be regarded as vitamins proper. Among these are the citrovorum factor and possibly also folic acid.

The **citrovorum factor**, also known as leucovorin³ or folic acid SF^{4,5}, was first described by SAUBERLICH and BAUMANN² in 1948. It is an essential growth factor for the organism *Leuconostoc citrovorum*; for *Streptococcus faecalis* it can be replaced by folic acid. The citrovorum factor has been identified by FLYNN et al.⁶ with their synthetic 5-formyl-5:6:7:8-tetrahydropteroylglutamic acid⁷ and appears to be the sole directly acting vitamin of the group. It occurs in yeast and liver and since it is replaceable by other substances of the group in test bacteria and animals (except in *Leuconostoc citrovorum*) was probably determined in the past as "folic acid".

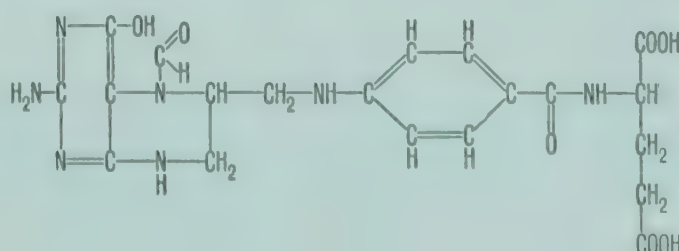
Pteroylglutamic acid (folic acid) has been known for a longer time and occurs likewise in yeast and liver. It appears to be the direct precursor of the citrovorum factor since the conversion of pteroylglutamic acid into 5-formyl-5:6:7:8-tetrahydropteroylglutamic acid is inhibited by folic acid antagonists, such as aminopterin, while the citrovorum factor in turn inhibits the antagonistic effect of aminopterin^{8–12}. Pteroylglutamic acid is identical with the *Lactobacillus casei* (liver) factor of SNELL and

PETERSON¹³ and with the vitamin Bc (chicks) of HOGAN and PARROT¹⁴. It is sparingly soluble in water, insoluble in fat solvents, stable to heat in neutral and alkaline solutions, unstable in acid solutions. The sodium salt is water-soluble. Pteroylglutamic acid is inactivated and decomposed by light, yielding xanthopterin aldehyde, then 2-amino-4-hydroxy-6-carboxypteridine and finally 2-amino-4-hydroxypteridine¹⁵.

Similar vitamin activity is shown by the widely occurring conjugates of pteroylglutamic acid: *pteroyltriglutamic acid* (also known as *teropterin*) is identical with the *Lactobacillus casei* (fermentation) factor and *pteroylheptaglutamic acid* is identical with the vitamin Bc conjugate from yeast. They are distinguished from pteroylglutamic acid by having respectively 2 and 6 further peptidic glutamic acid groups attached to the complex.

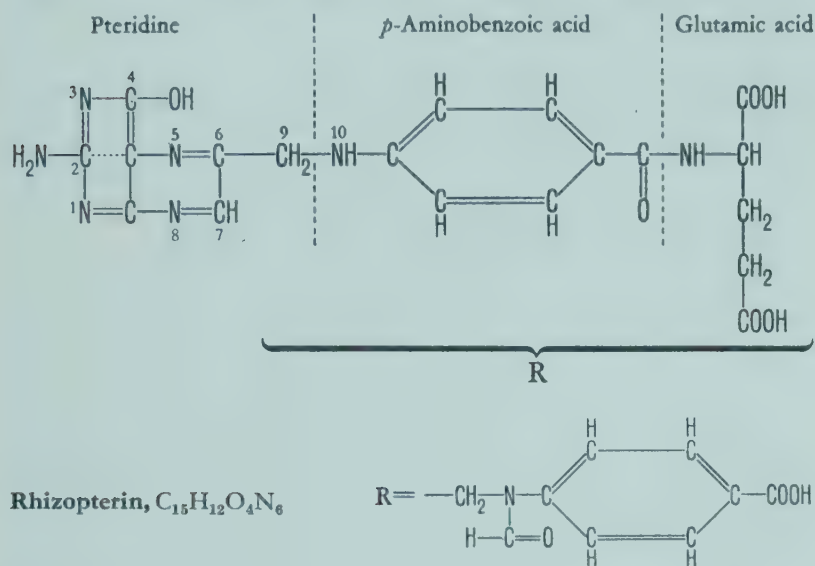
Similar but much weaker activity is also shown by *rhizopterin* (identical with the SLR factor of KERESZTESY et al.¹⁶) and by *xanthopterin*, the colouring matter isolated from butterflies by SCHÖPF and BECKER¹⁷.

Citrovorum factor, 5-formyl-5:6:7:8-tetrahydropteroylglutamic acid
C₂₀H₂₃O₇N₇; Mol. wt. 473.46



Folic acid, pteroylglutamic acid, $C_{19}H_{19}O_6N_7$

Mol. wt. 441.42; orange-yellow needles or platelets, tasteless, odourless



Xanthopterin, $C_6H_5O_2N_5$

R = —OH

Unit

No international unit; by weight.

Methods of test and assay

Citrovorum factor: *Leuconostoc citrovorum*. Folic acid, citrovorum factor and other substances with folic acid activity: *Streptococcus faecalis* and *Lactobacillus helveticus* (casei).

Occurrence

Citrovorum factor and folic acid: yeast and liver; **pteroylglutamic acid conjugates:** yeasts and other fungi, green leaves, grass, milk (very little); **rhizopterin:** liver, milk and cereal grains, very little in green leaves; **xanthopterin:** fish liver.

Physiology and function

Folic acid. Synthesized in large quantities by the intestinal flora. The organism appears to be able to meet its needs very largely from this synthesis; on the one hand a diet deficient in folic acid hardly affects the excretion in urine, on the other hand about 75% of the folic acid ingested is excreted in the urine¹⁸. On a normal diet the urinary excretion of folic acid amounts to 0.9–4.3 mg per 24 hours, mean 3.0¹⁸.

In health the gastric juice converts pteroylheptaglutamic acid into another unknown conjugate, a capacity which is lost in pernicious anaemia but not in sprue¹⁹. The blood contains folic acid conjugase²⁰, an enzyme which converts folic acid conjugates, provided they contain at least 3 glutamic acid groups, into folic acid. The folic acid conjugates therefore do not need to be converted in the intestinal tract for them to be utilizable by the organism. The blood level of this enzyme is not significantly lower in pernicious anaemia²⁰. Folic acid, or the citrovorum factor formed from it, appears to be essential for the oxidation of aromatic amino-acids and their metabolites. In premature births,

for example, folic acid lowers the urinary excretion of hydroxyphenyl derivatives²¹.

Folic acid deficiency in warm-blooded animals leads to interrupted growth and disturbance of the haematopoiesis (anaemia, leucopenia, granulocytopenia), also to depigmentation in rats, feather deficiencies in chicks, diarrhoea and oedemas in monkeys.

Folic acid antagonists. A number of folic acid antagonists have been synthesized by substitution in the pteroyl group. The best known are 4-aminopteroylglutamic acid (aminopterin), 4-amino-N¹⁰-methylpteroylglutamic acid (amethopterin) and 4-aminopteroylaspartic acid, all of which are toxic. All these folic acid antagonists inhibit the vitamin activity of pteroylglutamic acid and its conjugates, of rhizopterin and of xanthopterin with respect to all experimental animals and bacteria, but have no effect on the activity of the citrovorum factor.

Citrovorum factor. The fact that the activity of the citrovorum factor is not inhibited by folic acid antagonists and that furthermore it has weight for weight the same activity as folic acid^{22,23}, leads to the conclusion that it is the direct haemopoietically active substance of the folic acid group and that folic acid itself should be regarded as the precursor of the citrovorum factor, and the folic acid conjugates and the other members of the group as the precursors of folic acid. The conversion of folic acid into 5-formyl-5:6:7:8-tetrahydropteroylglutamic acid (citrovorum factor) takes place in the liver, with the apparent participation of vitamins C and B₁₂^{24–26}.

Folic acid group and haematopoiesis

The citrovorum factor, or its precursors folic acid and folic acid conjugates, are essential for the maturation of the blood cells. They are the only substances which can effectively convert a pathological megaloblastic bone marrow into a normoblastic one²⁷. In pernicious anaemia the citrovorum factor is effective (without vitamin B₁₂) in parenteral doses of 0.75–3 mg over 10 days^{28–32}, in megaloblastic anaemia of children in parenteral doses of 75 µg/day³³. Folic acid is likewise fully effective in all megaloblastic anaemias other than pernicious, in which case it cannot quite normalize the blood picture and has no effect on the neurological symptoms.

Therapeutic application

Citrovorum factor in all megaloblastic anaemias, folic acid likewise (sprue, pellagra, coeliaca, goat's milk anaemia, pregnancy, alimentary megaloblastic anaemias), but not in pernicious anaemia. Since the relationship of the folic acid group to vitamin B₁₂ and the other vitamins of the B complex has not been elucidated it is advisable to support or complement folic acid therapy by administration of the whole B complex or of vitamin B₁₂: in folic acid therapy cases have been observed in which neuritis, for example, has developed during the treatment. This has been ascribed to a disturbance of the vitamin-B balance³⁴ (cf. similar B-complex disturbances under vitamin B₁). Folic acid antagonists: temporary success in leukaemia.

¹) MITCHELL et al., *J. Amer. chem. Soc.*, **63**, 2284, 1941; *ibid.*, **66**, 267, 1944. ²) SAUBERLICH and BAUMANN, *J. biol. Chem.*, **176**, 165, 1948. ³) BROCKMAN et al., *J. Amer. chem. Soc.*, **72**, 4325, 1950. ⁴) SHIVE et al., *ibid.*, **72**, 2817, 1950. ⁵) POHLAND et al., *ibid.*, **73**, 3247, 1951. ⁶) FLYNN et al., *ibid.*, **73**, 1979, 1951. ⁷) COSULICH et al., *ibid.*, **73**, 5006, 1951. ⁸) BROQUIST et al., *J. biol. Chem.*, **185**, 399, 1950. ⁹) SAUBERLICH, H. E., *Arch. Biochem.*, **24**, 224, 1949; *Fed. Proc.*, **8**, 247, 1949. ¹⁰) NICOL and WELCH, *Proc. Soc. exp. Biol.*, **74**, 403, 1950. ¹¹) CRAVEN et al., *ibid.*, **75**, 43, 1950. ¹²) CARTWRIGHT et al., *ibid.*, **78**, 563, 1951. ¹³) SNELL and PETERSON, *J. Bact.*, **36**, 273, 1940. ¹⁴) HOGAN and PARROT, *J. biol. Chem.*, **132**, 507, 1940. ¹⁵) LOWRY et al., *ibid.*, **180**, 389, 1949. ¹⁶) KERESZTESY et al., *Science*, **97**, 465, 1943. ¹⁷) SCHÖPF and BECKER, *Annalen*, **524**, 49, 124, 1936. ¹⁸) JOHNSON and PARSONS, *Fed. Proc.*, **10**, 385, 1951. ¹⁹) BUYZE and ENGEL, *Nature*, **163**, 135, 1949. ²⁰) WOLFF et al., *Science*, **109**, 612, 1949. ²¹) GOVAN and GORDON, *ibid.*, **109**, 332, 1949. ²²) CALLENDER and LAITHER, *J. clin. Path.*, **4**, 204, 1951. ²³) WOODRUFF et al., *Proc. Soc. exp. Biol.*, **77**, 16, 1951. ²⁴) NICOL and WELCH, *ibid.*, **74**, 52, 1950. ²⁵) DIETRICH et al., *ibid.*, **77**, 93, 1951. ²⁶) GABUZDA et al., *J. clin. Invest.*, **30**, 639, 1951. ²⁷) MEYER et al., *Amer. J. med. Sci.*, **218**, 197, 1949. ²⁸) SPIES et al., *Sth. med. J. (Bgham, Ala.)*, **43**, 1076, 1950. ²⁹) MEYER et al., *Proc. Soc. exp. Biol.*, **76**, 86, 1951. ³⁰) ELLISON et al., *ibid.*, **76**, 366, 1951. ³¹) DAVIDSON and GIRDWOOD, *Lancet*, **1**, 722, 1951. ³²) JARROLD et al., *Science*, **113**, 688, 1951. ³³) WOODRUFF et al., *Proc. Soc. exp. Biol.*, **77**, 16, 1951. ³⁴) DAVIDSON and GIRDWOOD, *Lancet*, **1**, 360, 1948.

Vitamin B₁₂¹

Cobalamin, Cyanocobalamin (B. P.), Anti-pernicious anaemia factor (WEST), Extrinsic factor (CASTLE), Animal Protein Factor = APF, Zoopherin (ZUCKER and ZUCKER), *Lactobacillus lactis* DORNER Factor (SHORB), *Lactobacillus leichmanni* Factor (SKEGGS et al.), Hatchability Factor (BETHKE), Cow Manure Factor (RUBIN and BIRD), Nutritional Factor X (HARTMANN).

Vitamin B₁₂ occurs in a number of forms, B₁₂, B₁₂b⁽²⁾, B₁₂c, B₁₂d; a further form B₁₂a⁽³⁾ arises from the effect of light on catalyzed B₁₂ in aqueous solution. All these forms possess very similar physical and chemical properties and biological activity⁴, except B₁₂a⁽⁵⁾ which presumably does not occur naturally and has a biological activity only 1/6 to 1/2 of that of B₁₂. Vitamin B₁₂ is hygroscopic, stable in neutral aqueous solutions at room temperature, relatively stable to boiling in aqueous solution, unstable in alkaline or boiling acid solutions. The various forms of B₁₂ can be separated chromatographically. The constitution of B₁₂ has recently been elucidated^{6, 7}:

Vitamin B₁₂, C₆₃H₉₀N₁₄O₁₄PCo

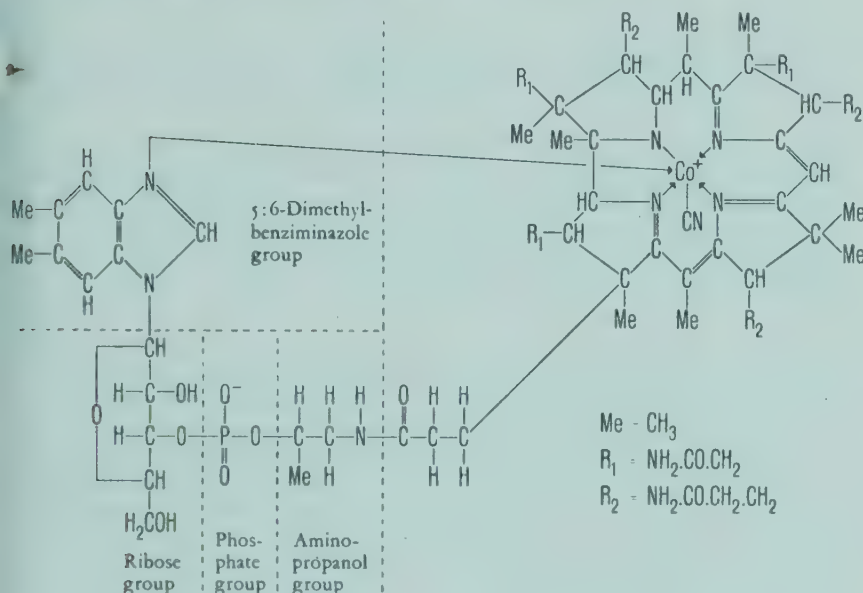
Mol. wt. 1357.44

M. p. < 300 °C^(8, 9)

Red crystals, blackening at 190–215 °C^(8, 9)

Absorption maxima in water 2780 Å (B₁₂b 2730 Å)

3610 Å (B₁₂b 3510 Å), 5500 Å (B₁₂b 5250 Å)⁽⁹⁾ laevo-rotatory⁽⁹⁾



Unit

No international unit as yet. 1 µg vitamin B₁₂ = 11,000 LLD units (*Lactobacillus lactis* DORNER units) = 1 U.S. Pharmacopeia (liver extract) unit (the USP unit is defined as that amount which produces, when administered daily, satisfactory clinical and haematopoietic responses in Addisonian pernicious anaemia). The activity of 1000 LLD units corresponds to that of about 1 ml of a good liver extract.

Methods of test and assay

Curative tests on higher animals. Microbiologically by means of *Lactobacillus lactis* DORNER or *L. leichmanni* (these tests have been recently shown to be not strictly specific¹⁰). In pure solutions also spectrometrically. Separation of B₁₂, B₁₂b, B₁₂c, B₁₂d chromatographically; chemically after BOXER and RICHARDS¹¹.

Occurrence¹ (values in µg B₁₂ activity/100 g weight dry, unless otherwise stated)

In sharp contrast to the other vitamins of the B complex, B₁₂ does not occur (or occurs in quantities of insignificant activity) in the higher plants. It is, however, present in all animal tissues and is synthesized only by micro-organisms, mainly lower fungi. The upper layers of the soil are rich in vitamin B₁₂, as also is animal excrement, particularly that of poultry.

Streptomyces aureofaciens (cells) 1000–1300; *Bacillus megatherium* (whole cultures) 40–80; stomach contents (rumen) of sheep: protozoal fraction (cells) 630, bacterial fraction (cells) 200; stomach flora cultivated on sterile gastric juice (cells) 400; pig's liver 180; calf liver 240; fish meal¹², up to 260; beef muscle¹² 30–100; calf spleen 93; calf thymus 24; pork (shoulder) 10 (100 g weight fresh); meat meal 10; oysters (shelled) 28; milk 1.1–1.25 per 100 ml; casein¹² 104; earthworms 110; upper layers of the soil 170.

Physiology and function

B₁₂ is active in extraordinary small quantities (in relapses of pernicious anaemia parenteral doses of 1 µg/day¹⁴ are fully effective) and is stored in the animal organism to such an extent that it is, for example, almost impossible to produce in a short space of time an alimentary B₁₂-deficiency in second-generation rats if the females of the first generation were not kept on a B₁₂-deficient diet.

B₁₂ is synthesized in large quantities by the intestinal flora. However it is doubtful whether any of this product is absorbed since animals on a B₁₂-deficient diet must have access to excrement if they are not to develop B₁₂-deficiency.

In chickens B₁₂-deficiency results in a high mortality rate in the embryos shortly before or after hatching (hence the name Hatchability Factor), the surviving chicks showing defective growth and retarded development. The fertility is unaffected and there are no particular pathological changes. The same applies to rats: high mortality of suckling animals, retarded growth.

B₁₂-Deficiency can be produced by a purely vegetable diet or by a mixed diet containing alcohol-extracted casein (hence the name Animal Protein Factor). The deficiency symptoms appear much more quickly if the (purified) protein component of the diet is increased, or if a deficiency of compounds supplying methyl groups (methionine, choline) is created, or if substances with thyroid activity are included in the diet. It follows that B₁₂ stands in close relationship to protein metabolism and is necessary for transmethylation processes (but is not replaceable by methionine or choline). It also follows that human pernicious anaemia, as a deficiency disease of endogenous origin, is probably related to the metabolism of the cell nucleus (presumably through nucleic acid synthesis, although administration of nucleic acids is not a substitute for B₁₂).

In pernicious anaemia, B₁₂ is only fully effective parenterally; orally it is only fully effective with simultaneous administration of the gastric juice of healthy subjects¹⁵ (optimal 25–150 ml with a B₁₂ dosage of 5 µg/day)¹⁶. According to TERNBERG and EAKIN¹⁷ gastric juice contains a protein, named apoerythroprotein, which combines specifically with B₁₂ to form erythroprotein. Presumably the latter undergoes readier resorption than B₁₂ or protects B₁₂ from decomposition by chemical or bacterial agents. Recent researches indicate that apoerythroprotein is identical with CASTLE's Intrinsic Factor²⁴. The gastric juice of patients with pernicious anaemia contains much reduced amounts of apoerythroprotein.

B₁₂ and other factors. Although the parallel effectiveness of B₁₂ and folic acid in the treatment of various megaloblastic anaemias and sprue indicates a mutual replaceability, this is in fact not the case. They are both essential to the organism and can only replace each other in cases of combined "deficiencies", i.e. when the administration of both is minimal, larger amounts of the one vitamin can improve the condition due to the deficiency of both. For this reason the combined administration of B₁₂ and folic acid (particularly in anaemias due to alimentary deficiencies) is often more effective than either vitamin alone. On the other hand the citrovorum factor always appears to be effective when administered alone.

B₁₂ is an important growth factor and it is therefore of interest that the Animal Protein Factor (APF) usually identified with it is in some species not entirely replaceable by B₁₂. Thus it has been shown in pigs¹⁷ and chickens¹⁸ that APF-deficiency is only partly relieved by B₁₂ and that a further substance is necessary for complete cure. This substance has been identified as chlortetracyclin. Another antibiotic, streptomycin, has also been shown to be a growth factor¹⁹. Since, however, as regulators of the intestinal flora these substances do not participate directly in metabolism they are not to be classed as vitamins and are not biochemically related to B₁₂ (except in respect of their common synthesis by a micro-organism), although the discovery of their growth-promoting effect is due to research on vitamin B₁₂.

Therapeutic application

With or without folic acid or citrovorum factor, according to results: in all megaloblastic anaemias (pernicious anaemia, including that of pregnancy, megaloblastic anaemia after gastrec-

tomy²⁰ and of infants²¹, goat's milk anaemia, anaemia due to alimentary deficiency²², tropical and infantile sprue²², alimentary glossitis²², interrupted growth due to undernourishment²³).

Reviews. General: SMITH, E. L., *Nutr. Abstr. Rev.*, **20**, 795, 1951; clinical: UNGLEY, C. C., *ibid.*, **21**, 1, 1951.

¹) See also: ZUCKER and ZUCKER, *Vitam. and Horm.*, **8**, 1950. ²) PIERCE et al., *J. Amer. chem. Soc.*, **71**, 2952, 1949. ³) KACZKA et al., *ibid.*, **71**, 1514, 1949. ⁴) UNGLEY and CAMPBELL, *Brit. med. J.*, **1**, 152, 1951, and MARSHALL and CHALMERS, *ibid.*, **1**, 161, 1951. ⁵) WOLF et al., *Amer. chem. Soc., 116th Meeting, Abstracts*, 32, 1949. ⁶) HODGKIN et al., *Nature*, **176**, 325, 1955. ⁷) TODD et al., *Nature*, **176**, 328, 1955. ⁸) RICKES et al., *Science*, **108**, 634, 1948. ⁹) BRINK et al., *J. Amer. chem. Soc.*, **71**, 1854, 1949. ¹⁰) SKEGGS et al., *J. biol. Chem.*, **176**, 1459, 1948, and GREEVE et al., *J. biol. Chem.*, **178**, 999, 1949. ¹¹) BOXER and RICHARDS, *Arch. Biochem.*, **30**, 372, 382, 392, 1951. ¹²) PEELER et al., *J. Nutr.*, **43**, 49, 1951. ¹³) SCHWEIGERT et al., *Fed. Proc.*, **10**, 394, 1951. ¹⁴) REISNER and WEST, *Proc. Soc. exp. Biol.*, **71**, 651, 1949. ¹⁵) SPIES et al., *Sth. med. J. (Bgham, Ala.)*, **42**, 528, 1949. ¹⁶) HALL et al., *Proc. Mayo Clin.*, **24**, 99, 1949. ¹⁷) JUKES et al., *Arch. Biochem.*, **26**, 324, 1950, and BURNSIDE et al., *Proc. Soc. exp. Biol.*, **74**, 173, 1950. ¹⁸) STOKSTAD and JUKES, *Amer. chem. Soc., 117th Meeting*, 12, 1950. ¹⁹) LUECKE et al., *Arch. Biochem.*, **26**, 326, 1950. ²⁰) CONWAY and CONWAY, *Brit. med. J.*, **1**, 158, 1951. ²¹) MCPHERSON et al., *J. Pediat.*, **34**, 529, 1949. ²²) SPIES et al., *Blood*, **4**, 819, 1949. ²³) WETZEL et al., *Science*, **110**, 651, 1949. ²⁴) BEERSTECHER, E., *Fed. Proc.*, **10**, 161, 1951.

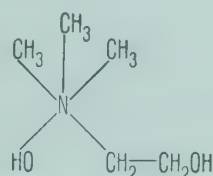
On this and the following page will be found descriptions of those vitamins which are distinguished from the others by the considerably larger amounts in which they occur, and which for this reason are better classed with the amino-acids as "essential foods". These vitamins are choline and inositol, at present classed with the B complex although they are biologically unrelated to it, and the essential unsaturated fatty acids known as vitamin F which should be classed with the fat-soluble vitamins.

Choline

This substance is a strong organic base which occurs in nature as a component of certain phospholipids (particularly lecithin) or as acetylcholine. Choline is soluble in water and alcohol, insoluble in ether, benzene and carbon disulphide. It is stable to heat in acid solutions, unstable in alkaline solutions; extremely hygroscopic.

Choline, C₅H₁₅O₂N

Mol. wt. 121.13
White crystals
Corrosive, bitter taste

**Unit**

None; by weight.

Methods of test and assay

Chemically by precipitation of the reineckate¹, microbiologically by means of strains of *Neurospora crassa* irradiated by ultraviolet light². For determination in the presence of the whole B complex, see BANDELIN and TUSCHOFF³.

Occurrence (values are in mg per 100 g weight fresh, unless otherwise stated)

The best sources of choline are eggs, meat and legumes, followed by cereal- and dairy-products. Vegetables contain little or none, fruit mostly none. There is no loss in cooking.

Eggs: yolk 1713, white very little. **Meat**: liver of various species 350–650, kidneys 300, muscle 70–140. **Fish**: cod 200, salmon 180, herring 127, trout 87. **Legumes**: soya beans 237, dried beans 181, garden peas 55, dried peas 188. **Cereals**: wheat germ 400, oat flakes 151, barley 139, polished rice 88, black bread 56, white flour 52. **Dairy products**: dried whole milk 170, cheese 50, milk 14.7/100 ml. **Vegetables and edible fungi**: Brussels sprouts 103, radishes 48, spinach 38, mushrooms 20–70, celery 17, parsley 16, carrots 4; none in potatoes, onions or tomatoes. **Fruit**: none in apples, plums, melons or grapes.

Physiology and function

The daily intake on a normal diet amounts to 500–1000 mg, average 646 mg, corresponding to a requirement (assumed) per day of ca. 9 mg/kg body weight. The urinary excretion is 5.6–9.0 mg

per 24 hours, the serum level 0.3–1.5 mg/100 ml (after SCHLEGEL, J. U., *Proc. Soc. exp. Biol.*, **70**, 695, 1949).

Choline has an important role as donator of methyl groups in transmethylation processes such as, for example, methionine → creatine, choline → methionine and vice versa, betaine → choline, nicotinamide → N¹-methylnicotinamide, etc. In this role it can be partially replaced by methionine and betaine as well as by vitamin B₁₂.

Choline can be synthesized by the organism itself in sufficient quantities, provided that sufficient other donators of methyl groups are available.

In animals, choline deficiency results in fatty infiltration of the liver (particularly in growing animals under certain diets, such as those rich in fats or carbohydrates) and in renal necrosis (the latter only in very young, rapidly growing animals). The choline requirement depends very largely on the protein composition and the other vitamins of the diet, particularly vitamin B₁₂. The latter can reduce the choline requirement very markedly, in dogs to nil⁵. In toxic fatty degeneration of the liver choline can also exercise a certain protective action. In this respect, however, it is greatly exceeded by vitamin E and particularly by proteins.

Pharmacology

As precursor of acetylcholine, choline also possesses a vasodilator activity, but to a much smaller degree.

Therapeutic application

In liver-protective diets, insofar as sufficient adequate proteins cannot be administered, but always in combination with other vitamins of the B complex, particularly vitamin B₁₂ and vitamin E.

Reviews on lipotropic substances: HENRY and PATTERSON, *Physiol. Rev.*, **24**, 128, 1944; DOLAN, R. A., *Minn. Med.*, **31**, 1198, 1948; BEST, C. H., *Diabetes and Insulin and the Lipotropic Factors*, Springfield, 1948; SHERLOCK, S., *Liver Disease*, London, 1951. **Treatment of severe liver diseases**: SESSIONS, J. T., *Med. Clin. N. Amer.*, **35**, 1441, 1951.

¹) BEATTIE, F. J. R., *Biochem. J.*, **30**, 1554, 1936; JACOBI et al., *J. biol. Chem.*, **138**, 571, 1941; ENGEL, R. W., *ibid.*, **144**, 701, 1942; GLICK, D., *ibid.*, **156**, 643, 1944. ²) HOROWITZ and BEADLE, *J. biol. Chem.*, **150**, 325, 1943; LUECKE and PEARSON, *ibid.*, **153**, 259, 1944; **155**, 507, 1944. ³) BANDELIN and TUSCHOFF, *J. Amer. Ass. Sci.*, **40**, 245, 1951. ⁴) JUKES and STOKSTAD, *J. Nutr.*, **43**, 459, 1951. ⁵) BURNS and MCKIBBIN, *ibid.*, **44**, 487, 1951.

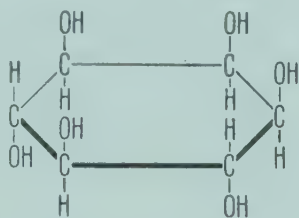
Bibliography: The data in the section "Vitamins" have been based on the following literature, in addition to that cited in the text: ABDERHALDEN, E., *Physiologische Chemie*, Basel, 1948; BICKNELL and PRESCOTT, *The Vitamins in Medicine*, London, 1946; CLARK, G. W., *A Vitamin Digest*, Springfield, 1953; GYORGY, P., et al., *Vitamin Methods*, New York, 1950–51; CONN et al., *Current Therapy*, Philadelphia, 1955; HOTZEL, A., *Vitamine und Vitaminpräparate*, Aulendorf, 1949; SUNDERMAN and BOERNER, *Normal Values in Clinical Medicine*, Philadelphia, 1950; GROSSE-BROCKHOFF, *Pathologische Physiologie*, Berlin, 1950; LEHNARTZ, E., *Chemische Physiologie*, Berlin, 1948; KARRER, P., *Lehrbuch der organischen Chemie*, Stuttgart, 1950; ROBINSON, F. A., *The Vitamin B Complex*, New York, 1951; *Vitam. and Horm.*, 1949–52; *Z. Vitaminforsch.*, 1948–53; *J. Nutr.*, 1949–53; *Ann. Rev. Biochem.*, 1950–53.

*meso*Inositol

This substance occurs in nature either in the free form or in various combinations such as phytin, liposterol, etc. It is soluble in water, insoluble in organic solvents, stable to acids and alkalis.

*meso*Inositol, $C_6H_{12}O_6$

Mol. wt. 180.16
 M. p. 225–226°C
 White crystals
 Sweet taste



Of the eight possible *cis-trans*-isomers with the inositol structure, the optically-active (+)- and (–)-cyclitols, the racemic form and other isomers occur naturally. The configuration of *meso*-inositol was determined in 1942 by POSTERNAK and FISCHER (cf. FIESER and FIESER, *Organic Chemistry*, 2nd ed., London, 1953, page 522).

Unit

None; by weight.

Methods of test and assay

Chemically¹, biologically by means of white mice², microbiologically by means of *Saccharomyces cerevisiae*³, *S. carlsbergensis*⁴, *Neurospora crassa*⁵, *Kloeckera brevis*⁶, etc.

Occurrence (values are in mg per 100 g weight fresh, unless otherwise stated).

Yeast 500, crude liver extracts 200–300, beef liver 340, beef brain 149, white flour 110, oats 100, black bread 64, milk 50/100 ml. In muscle inositol is presumably linked with a protein, in brain it

is present in the phospholipid cephalin as diphosphoinositide. In plants it is mostly found as phytin, the acid calcium magnesium salt of phytic acid (the hexaphosphoric ester of inositol). It also occurs as the mono- and tri-phosphoric ester.

Physiology and function

Under normal conditions inositol is eliminated to the extent of 15 mg/24 hours in urine and 0.648 mg/24 hours in sweat⁷. The plasma level amounts to 0.37–0.76 mg/100 ml⁸. The daily requirement in man is estimated at 1 mg per 2500 calories⁹.

Inositol deficiency in mice and rats results in loss of weight and alopecia¹⁰, in dogs in diminished peristalsis of stomach and jejunum¹¹. In rats inositol has a lipotropic action, *but only on a fat-free diet*¹²; it is effective against cholesterol infiltration but ineffective against infiltration of neutral fats. The lipotropic action has also been observed in patients with carcinoma of the gastrointestinal tract¹².

The high phytic acid content of many cereals is important inasmuch as phytic acid forms with calcium an insoluble salt in which neither the calcium nor the phosphorus is available to the organism. The calcium of many cereals is therefore completely or partly useless to the organism. The phytic acid of cereals can also immobilize the calcium ingested with other foods, such as milk. Oats, as well as other cereal products, therefore exhibit a marked rachitogenic activity. Yeast fermentation destroys phytic acid, so that bakery products made with yeast are not rachitogenic. Iron is also immobilized by phytic acid, but not to the same extent as calcium.

Therapeutic application

As lipotropic substance in experimental therapy.

¹) GREGORY, R. A., *Biochem. J.*, **29**, 2798, 1935. ²) WOLLEY, D. W., *J. biol. Chem.*, **136**, 113, 1940; **139**, 29, 1941; *J. Nutr.*, **21**, Suppl., 17, 1941; ³) WOLLEY, D. W., *J. biol. Chem.*, **140**, 453, 1941; *J. exp. Med.*, **75**, 277, 1942. ⁴) ATKIN et al., *Ind. Eng. Chem., Anal. Ed.*, **15**, 141, 1943. ⁵) BEADLE, G. W., *J. biol. Chem.*, **156**, 683, 1944. ⁶) BURKHOLDER et al., *J. Bact.*, **48**, 385, 1944. ⁷) JOHNSON et al., *J. biol. Chem.*, **161**, 357, 1945. ⁸) SONNE and SOBOTKA, *Arch. Biochem.*, **14**, 93, 1947. ⁹) WILLIAMS, R. J., *J. Amer. med. Ass.*, **119**, 1, 1942. ¹⁰) WOLLEY, D. W., *Science*, **92**, 384, 1940. ¹¹) MARTIN et al., *Amer. J. dig. Dis.*, **8**, 290, 1941; **9**, 268, 1942. ¹²) ABELS et al., *Proc. Soc. exp. Biol.*, **54**, 157, 1943. ¹³) BEST, C. H., *Diabetes and Insulin and the Lipotropic Factors*, Springfield, 1948.

Vitamin F

The name vitamin F is used to designate certain essential unsaturated fatty acids (linoleic, linolenic, arachidonic, clupanodonic acids, etc.).

Linoleic acid $CH_3.(CH_2)_3.(CH_2.CH:CH)_2.(CH_2)_7.COOH$
 colourless oil

Linolenic acid $CH_3.(CH_2.CH:CH)_3.(CH_2)_7.COOH$
 colourless oil

Arachidonic acid $CH_3.(CH_2)_3.(CH_2.CH:CH)_4.(CH_2)_3.COOH$

Unit. None.

Methods of test and assay. Chemically.

Occurrence

In all fats, particularly vegetable fats: (% unsaturated fatty acids, after BICKNELL and PRESCOTT, *Vitamins in Medicine*, London, 1946) wheat germ oil 44–52, cottonseed oil 35–50, arachis oil 13–27, olive oil 4–14, bacon fat 5–11, butter 1.9–4, milk 0.15–0.23, liver oils 0.

Physiology and function

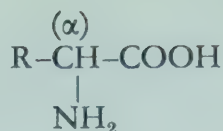
Not all highly unsaturated fatty acids possess “vitamin” activity; the principal ones with such activity are given opposite. The essential fatty acids are stored mainly in the phospholipids and are very sparingly utilized by the body. Even in cases of very severe deficiency of fats lasting over a year the vitamin-F reserve in the liver does not fall below 50%. In rats, mice and dogs vitamin-F deficiency causes a slowing-down and eventual stoppage of growth accompanied by increased B.M.R., disturbances of fat and water balance, pathological changes in skin and hair, degeneration of the kidneys and loss of sexual function. Vitamin F has an economizing effect on pyridoxine and vice versa. It has been shown that the individual active fatty acids in the organism have no uniform role.

Therapeutic application

In eczema and burns, as lipotropic substance.

For a review see STANGL, E., *Z. Vitaminforsch.*, **23**, 164, 1951.

Amino-acids are fatty acids in which one of the H-atoms attached to the carbon chain has been replaced by an amino-group (NH₂). All naturally-occurring amino-acids except β-alanine are α-acids according to the formula:



With the sole exceptions of glycine and β-alanine they all possess an asymmetrically substituted C-atom and are therefore optically active. The prefix D or L indicates the configurational family of the α-C-atom. The direction of optical rotation is indicated by (+) or (-). The designation **essential** refers only to *man*¹. The data on *taste* are from CROCKER².

Monoaminomonocarboxylic acids				Diaminomonocarboxylic acids			
Name	Structure	Name	Structure	Name	Structure	Name	Structure
Glycine or Glycocol Aminoacetic acid <i>Sweet taste</i>	$\begin{array}{c} \text{CH}_2-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	D(-)-Threonine α-Amino-β-hydroxybutyric acid Essential	$\begin{array}{c} \text{CH}_3 \\ \\ \text{HO}-\text{C}-\text{H} \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	L(+)-Ornithine αδ-Diaminovaleric acid	$\begin{array}{c} \text{CH}_2-\text{NH}_2 \\ \\ \text{CH}_2 \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	L(+)-Arginine α-Amino-δ-guanidino- <i>n</i> -valeric acid	$\begin{array}{c} \text{NH}_2 \\ \\ \text{CH}_2-\text{NH}-\text{C} \\ \\ \text{NH} \\ \\ \text{CH}_2 \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$
Sarcosine Methylglycocol	$\begin{array}{c} \text{CH}_2-\text{NH}-\text{CH}_3 \\ \\ \text{COOH} \end{array}$	L(+)-Valine α-Amino <i>iso</i> valeric acid Essential	$\begin{array}{c} \text{CH}_3 \quad \text{CH}_3 \\ \quad \\ \text{CH} \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	Citrulline α-Amino-δ-ureido- <i>n</i> -valeric acid	$\begin{array}{c} \text{NH}_2 \\ \\ \text{CH}_2-\text{NH}-\text{C} \\ \\ \text{O} \\ \\ \text{CH}_2 \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	L(+)-Lysine αε-Diamino- <i>n</i> -caproic acid <i>Bitter taste</i> Essential	$\begin{array}{c} \text{CH}_2-\text{NH}_2 \\ \\ \text{CH}_2 \\ \\ \text{CH}_2 \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$
L(+)-Alanine α-Aminopropionic acid <i>Sweet taste</i>	$\begin{array}{c} \text{CH}_3 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	L(+)-Norvaline α-Amino- <i>n</i> -valeric acid	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_2 \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	L(-)-Aspartic acid Aminosuccinic acid <i>Bitter taste</i>	$\begin{array}{c} \text{COOH} \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	L(+)-Glutamine α-Amino-γ-carbamylbutyric acid	$\begin{array}{c} \text{CO}-\text{NH}_2 \\ \\ \text{CH}_2 \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$
β-Alanine β-Aminopropionic acid, the sole naturally-occurring β-amino-acid	$\begin{array}{c} \text{CH}_2-\text{NH}_2 \\ \\ \text{CH}_2 \\ \\ \text{COOH} \end{array}$	L(+)-Isoleucine α-Amino-β-methyl-β-ethylpropionic acid Essential	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_2 \\ \quad \\ \text{CH} \quad \text{CH}_3 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	L(-)-Asparagine α-Amino-β-carbamylpropionic acid	$\begin{array}{c} \text{CO}-\text{NH}_2 \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	β-Hydroxyglutamic acid α-Amino-β-hydroxyglutaric acid	$\begin{array}{c} \text{COOH} \\ \\ \text{CH}_2 \\ \\ \text{CHOH} \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$
L(-)-Serine α-Amino-β-hydroxypropionic acid	$\begin{array}{c} \text{CH}_2\text{OH} \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	L(+)-Norleucine α-Amino- <i>n</i> -caproic acid	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_2 \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	L(+)-Glutamic acid α-Aminoglutaric acid <i>Bitter taste</i> ³	$\begin{array}{c} \text{COOH} \\ \\ \text{CH}_2 \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$		
L(-)-Cysteine α-Amino-β-thiolpropionic acid	$\begin{array}{c} \text{CH}_2-\text{SH} \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	L(-)-Leucine α-Amino <i>iso</i> caproic acid Essential	$\begin{array}{c} \text{CH}_3 \quad \text{CH}_3 \\ \quad \\ \text{CH} \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	L(-)-Phenylalanine Essential	$\begin{array}{c} \text{H} \\ \\ \text{HC} \\ \quad \\ \text{HC} \quad \text{CH} \\ \quad \\ \text{C} \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	L(-)-Histidine α-Amino-β-glyoxalanylpropionic acid	$\begin{array}{c} \text{NH}_2 \\ \\ \text{CH}_2-\text{C}-\text{COOH} \\ \\ \text{H} \\ \\ \text{HC}=\text{C} \\ \quad \\ \text{HN} \quad \text{N} \\ \\ \text{H} \end{array}$
L(-)-Cystine 2:2'-Diamino-2:2'-dicarboxydiethyl sulphide	$\begin{array}{c} \text{CH}_2-\text{S}-\text{S}-\text{CH}_2 \\ \quad \quad \\ \text{H}-\text{C}-\text{NH}_2 \quad \text{H}-\text{C}-\text{NH}_2 \\ \quad \quad \\ \text{COOH} \quad \text{COOH} \end{array}$			L(-)-Tyrosine <i>p</i> -Hydroxyphenylalanine	$\begin{array}{c} \text{OH} \\ \\ \text{C} \\ \quad \\ \text{HC} \quad \text{CH} \\ \quad \\ \text{HC} \quad \text{CH} \\ \quad \\ \text{C} \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	L(-)-Proline 2-Carboxypyrrolidine	$\begin{array}{c} \text{H}_2\text{C}-\text{CH}_2 \\ \quad \\ \text{H}_2\text{C}-\text{CH}-\text{COOH} \\ \\ \text{H} \end{array}$
L(+)-α-Aminobutyric acid	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$			L(-)-Tryptophan α-Amino-β-3-indolylpropionic acid Essential	$\begin{array}{c} \text{H} \\ \\ \text{HC} \\ \quad \\ \text{HC} \quad \text{C} \\ \quad \quad \\ \text{HC} \quad \text{C} \quad \text{CH} \\ \quad \quad \\ \text{H} \quad \text{N} \quad \text{H} \\ \\ \text{C} \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$	L(-)-Hydroxyproline 4-Hydroxy-2-carboxypyrrolidine <i>Sweet taste</i>	$\begin{array}{c} \text{HOHC}-\text{CH}_2 \\ \quad \\ \text{H}_2\text{C}-\text{CH}-\text{COOH} \\ \\ \text{H} \end{array}$
L(-)-Methionine α-Amino-γ-methylthiobutyric acid <i>Bitter-sweet taste</i> Essential	$\begin{array}{c} \text{CH}_2-\text{S}-\text{CH}_3 \\ \\ \text{CH}_2 \\ \\ \text{H}-\text{C}-\text{NH}_2 \\ \\ \text{COOH} \end{array}$						

¹) ROSE, W. C., *Fed. Proc.*, **8**, 546, 1949; and ROSE et al., *J. Biol. Chem.*, **182**, 541, 1950; **188**, 59, 1951. ²) CROCKER and SJOISTROM, *Food Research*, **13**, 450, 1948.

³) Monosodium glutamate has at first a salty-sweet taste, then bitter-sweet. On the tongue it produces a slight burning sensation similar to that produced by anaesthetics. In the pure state it is odourless, the odour of commercial preparations being due to impurities.

	Isoleucine	Leucine	Lysine	Methionine	Phenylalanine	Threonine	Tryptophan	Valine
Cow's milk	5.86	9.20	8.52	2.65	4.75	4.34	1.36	7.12
	σ 0.080	σ 0.090	σ 0.148	σ 0.066	σ 0.040	σ 0.051		σ 0.067
Casein	6.1	9.2	8.2	2.8	5.0	4.9	1.2	7.2
α-Casein	6.4	7.9	8.9	2.5	4.6	4.9	1.6	6.3
β-Casein	5.5	11.6	6.5	3.4	5.8	5.1	0.65	10.2
Breast-milk casein	6.3	12.2	5.6	2.7	5.8	4.5	1.05	5.0
Gelatin	5.23		4.6	0.9	2.55	2.20	—	3.3
Beef muscle	5.5	7.6	8.6	2.5	3.9	4.8	1.19	5.4
Beef liver	4.8	8.4	6.6	2.2	4.8	4.2	1.52	5.9
Whole egg	6.7	9.2	7.3	3.1	5.4	5.3	1.6	7.1
Soya bean flour	5.0	7.5	5.7	1.3	4.9	3.8	1.46	5.0
Peas	4.6	6.6	5.7	0.69	4.7	4.0	0.81	5.0
Whole wheat	3.7	6.2	2.4	1.1	4.8	2.5	1.17	4.4
Whole maize	4.1	9.6	2.3	1.4	4.3	3.5	0.5	5.3
Sunflower seeds ²	3.5	4.1	4.6	—	2.9	3.0	1.1	3.9
Carrots	4.4	5.6	3.1	0.96	4.1	4.0	0.6	5.7
	σ 0.14	σ 0.072	σ 0.19	σ 0.07	σ 0.24	σ 0.12	σ 0.07	σ 0.24
Brussels sprouts	4.4	7.2	5.6	2.6	3.7	5.0	1.6	6.4
Broccoli	3.6	6.1	5.3	2.4	3.3	3.8	1.3	3.9

Amino-acids essential to man

(after ROSE, W. C., *Fed. Proc.*, 8, 546, 1949)

Essential

- Isoleucine
- Leucine
- Lysine
- Methionine
- Phenylalanine
- Threonine
- Tryptophan
- Valine

Non-essential

- Alanine
- Arginine
- Aspartic acid
- Citrulline
- Cystine
- Glutamic acid
- Glycine (glycocoll)
- Histidine
- Hydroxyproline
- Proline
- Serine
- Tyrosine

For structural formulae
see the preceding page

Minimum and recommended intake of essential amino-acids in food (for adults, when the diet contains sufficient nitrogen for the synthesis of the non-essential amino-acids):

	Minimum daily requirement	Recommended daily intake
	grams	grams
L-Isoleucine	0.70	1.4
L-Leucine	1.10	2.2
L-Lysine	0.80	1.6
L-Methionine	1.10	2.2
L-Phenylalanine	1.10	2.2
L-Threonine	0.50	1.0
L-Tryptophan	0.25	0.5
L-Valine	0.80	1.6

For diets poor in amino-acids the recommended, not the minimum, values should be used.

Amino-acid composition:

Breast milk	see page 228
Blood (free)	see page 317
Blood plasma proteins	see page 315
Urine	see pages 288 and 289

Remarks

Glycine (glycocoll, aminoacetic acid) represents the starting point of the synthesis of protoporphyrin in bone marrow, an essential part of the biosynthesis of haemoglobin. It is lacking in milk and in most albumins. In the organism it can be synthesized from serine and N-free precursors.

Alanine is a component of all proteins and can be synthesized in the organism from hydroxy- and keto-acids with 3 C-atoms.

Cysteine is extremely easily oxidized to cystine. The reversible reaction $\text{cysteine} \rightleftharpoons \text{cystine}$ appears to play a significant part in cell respiration.

Methionine is an important methyl-group donator (cf. Choline, page 222). In rats it exhibits a marked protective action on the liver.

Arginine is a constituent of all proteins and can be synthesized by the organism from CO₂ and ammonia.

Lysine is a constituent of all proteins with free amino-groups.

Glutamic acid acts on the grey cells of the brain as oxygen and nitrogen acceptor. Favorable results have been observed in mental deficiency and retarded mental development (ca. 4 × 3 g per day). The improvement is most marked in the first 6 months of the treatment, thereafter it is slower. The maximum effect is shown after one year. An actual improvement in the intelligence is not to be expected however; rather is it a question of a stimulation of mental activity within the limits of the existing intellectual capacity.

The frequency of psychomotor and epileptic attacks is also markedly reduced, but major epilepsy is unaffected.

Phenylalanine and **tyrosine** are constituents of all proteins. Thyroxine is synthesized by the organism from tyrosine via the mono- and di-iodo-derivatives.

Tryptophan can be converted in the organism into nicotinic acid (cf. page 217).

Histidine is not an essential amino-acid for man, whereas it is indispensable to rats and other animals.

¹⁾ After KEMMERER and ACOSTA, *J. Nutr.*, 38, 531, 1949; KUIKEN and PEARSON, *ibid.*, 39, 171, 1949; *J. Am. diet. Ass.*, 24, 940, 1948; TRISTRAM, G. R., *Advances in Protein Chemistry*, 5, 84, 1949; MEEKIN and POLIS, *ibid.*, 5, 202, 1949; LUGG, J. W. H., *ibid.*, 5, 230, 1949.
²⁾ The values are for amino-acid N as percentage of total-protein N.

From *Recommended Dietary Allowances, 1953*, Food and Nutrition Board, National Research Council, Washington, and other sources

(The values given apply to persons in normal health and living in a temperate climate)

	Age in years	Weight		Height		Calories ¹ kcal	Proteins g	Calcium g	Iron mg	Vitamins						
		lb.	kg	in.	cm					A ² I.U.	B ₁ ³ mg	B ₂ ³ mg	Nicotin- ic acid ³ mg	C mg	D I.U.	
Men	25	143	65	67	170	3200	65	0.8	12 ⁴	5000	1.6	1.6	16	75	} see 5	
	45	143	65	67	170	2900	65	0.8	12 ⁴	5000	1.5	1.6	15	75		
	65	143	65	67	170	2600	65	0.8	12 ⁴	5000	1.3	1.6	13	75		
Women.....	25	121	55	62	157	2300	55	0.8	12	5000	1.2	1.4	12	70	} see 5	
	45	121	55	62	157	2100	55	0.8	12	5000	1.1	1.4	11	70		
	65	121	55	62	157	1800	55	0.8	12	5000	1.0	1.4	10	70		
	(3rd trimester) (850 ml/day)					add 400	80	1.5	15	6000	1.5	2.0	15	100		400
						add 1000	100	2.0	15	8000	1.5	2.5	15	150		400
Infants ⁶	0- 1 month ⁷															
	1- 3 months	13	6	24	60	kg × 120	kg × 3.5 ⁸	0.6 ⁸	6	1500	0.3	0.4	3	30	400	
	4- 9 months	20	9	28	70	kg × 110	kg × 3.5 ⁸	0.8 ⁸	6	1500	0.4	0.7	4	30	400	
	10-12 months	22	10	30	75	kg × 100	kg × 3.5 ⁸	1.0 ⁸	6	1500	0.5	0.9	5	30	400	
Children ⁹	1-3	27	12	34	87	1200	40	1.0	7	2000	0.6	1.0	6	35	400	
	4-6	40	18	43	109	1600	50	1.0	8	2500	0.8	1.2	8	50	400	
	7-9	59	27	51	129	2000	60	1.0	10	3500	1.0	1.5	10	60	400	
Boys ⁹	10-12	78	35	57	144	2500	70	1.2	12	4500	1.3	1.8	13	75	400	
	13-15	108	49	64	163	3200	85	1.4	15	5000	1.6	2.1	16	90	400	
	16-20	139	63	69	175	3800	100	1.4	15	5000	1.9	2.5	19	100	400	
Girls ⁹	10-12	79	36	57	144	2300	70	1.2	12	4500	1.2	1.8	12	75	400	
	13-15	108	49	63	160	2500	80	1.3	15	5000	1.3	2.0	13	80	400	
	16-20	120	54	64	162	2400	75	1.3	15	5000	1.2	1.9	12	80	400	

¹⁾ The optimal calorie intake must suffice for specific needs. It should be calculated to maintain the normal appropriate body weight or growth under conditions of normal good health.

²⁾ The vitamin-A requirement is dependent on the ratio vitamin A/carotenes in the diet. The values in the table are based on the assumption that ca. two thirds of the vitamin A is consumed in the form of carotenes, and that the latter have only half, or less, the activity of vitamin A. Cf. Vitamin A, page 209.

³⁾ For adults (except pregnant and lactating women) receiving 2000 calories or less, 1 mg B₁ or 10 mg nicotinic acid is sufficient. Other vitamins of the B complex are also necessary but the exact demands are unknown. Diets rich in vitamins B₁ and B₂ and nicotinic acid usually contain sufficient of the other B vitamins.

⁴⁾ There is no reason to assume that adult men require less iron. The requirement is usually met by a normal diet.

⁵⁾ The need for supplemental vitamin D by vigorous adults leading a normal life seems to be minimal. For elderly persons and for persons (such as nuns) whose clothing shields them from sunlight or who for other reasons receive little sunlight, a small supplement is desirable.

⁶⁾ The absolute requirements of infants increase from month to month. On the other hand the (relative) requirement per unit of body weight, expressed in calories, diminishes from month to month.

⁷⁾ During the first months of life the demands of many nutrients are dependent on the development of the kidney-, intestinal and glandular functions. Specific values have therefore not been given.

⁸⁾ For mainly breast-fed infants the requirement of supplementary proteins and calcium is small (2-3 g proteins per kg body weight).

⁹⁾ The values given are those for children in the middle of each age group (2, 5, 8, 11 years, etc.) and of average weight and activity.

From *Recommended Dietary Allowances, 1953*, Food and Nutrition Board, National Research Council, Washington, and other sources

(continued)

- Fats** Little information is available on the human requirement of fat. Estimates are therefore based at present more on dietary habits than on physiological data. It is desirable that the intake of fats should meet 25–35% of the calorie requirement; 1% of the calories should come from unsaturated fatty acids (linoleic and arachidonic acids in natural fats). Where the need for calories is high, such as in very active persons consuming 4500 calories and in children and adolescents, it is desirable to increase the coverage of the calorie requirement by fats to 30–35%. Since many foods, such as meat, milk, cheese, nuts, etc., contain fats, only one-half to one-third of these percentages needs to be met by additional “obvious” fats such as butter, lard, cooking fats, etc. The most easily digested fats are butter and vegetable oils. Hydrogenated (hardened) oils have little biological value unless improved by the addition of unsaturated fatty acids and fat-soluble vitamins.
- Water** The normal daily requirement for adults is 2.5 litres (4.5 Imperial pints). An ordinary standard is one millilitre for each (kilo-) calorie of food. Much of this quantity is contained in foods. Under conditions of extreme heat or hard physical work the daily requirement can rise to 5–13 litres (9–23 Imperial pints). Water should be allowed *ad libitum*, since the sensation of thirst is usually an adequate guide to intake, except for infants and sick persons. Cf. Water and Electrolyte Balance, pages 295–300.
- Salt** The requirements of salt (sodium chloride) and water are closely connected. The average daily intake of salt for the normal adult is 7–15 grams, more than enough to meet normal requirements and sufficient for a water intake of up to 4 litres. In extreme sweating one gram of additional salt is required for each litre of water consumed over and above 4 litres. Under unusual conditions, such as hard physical work in a hot climate, 10–15 grams daily, or even more, may be required with meals or in drinking water. However, after acclimatization to heat the salt content of sweat is greatly reduced (from 2–3 g per litre to 0.5 g/litre) and the need for salt additional to that consumed in food almost disappears.
- Phosphorus** During the latter part of pregnancy and during lactation, as well as in the diet of children, the intake of phosphorus should be at least equal to that of calcium. In adults the phosphorus requirement is $1\frac{1}{2}$ times that of calcium. In general it can be assumed that a diet containing sufficient protein and calcium also contains sufficient phosphorus, since the common foods richest in calcium and protein are also the best sources of phosphorus.
- Iodine** The requirement of iodine is small, probably ca. 0.002–0.004 mg/kg body weight daily. This need is met by the regular use of iodized salt; its use in adolescence and pregnancy is especially important.
- Copper** The daily requirement of copper for adults is ca. 1–2 mg. Infants and children require ca. 0.05 mg/kg body weight. The requirement of copper is about one-tenth that of iron. A diet satisfying other demands usually contains sufficient copper.
- Vitamin K** The requirement of vitamin K is usually met by the synthesis by the intestinal flora, except in infants during the first few days after birth. It is therefore desirable to give the mother additional oral vitamin K during the later months of pregnancy, or parenterally shortly before the birth. Alternatively it should be given to the infant immediately after birth, although the former is preferable.
- Other vitamins** See under Vitamins, pages 209–223.

(and of cow's milk¹)

Values are in milligrams per 100 ml, unless otherwise stated

(For definition of normal range and standard deviation σ , see page 32)

	Mature milk (15 days to 20 months post partum)			Transitional milk (5–10 days post partum)			Colostrum (first 5 days post partum)		Cow's milk	
	Mean	Range		Mean	Range		Mean	Range	Mean	Range
Calories (kcal) ...	65	—		63	—		57	—	65	—
Specific gravity ..	1.031	1.026–1.037		1.035	1.034–1.036		—	—	1.031	—
Solids, total	12.4 g	10–17 g		13.6 g	10–16 g		12.8 g	10–17 g	12.7 g	8–20 g
Ash, total	0.21 g	0.1–0.5 g		0.24 g	0.1–0.4 g		0.33 g	0.2–0.7 g	0.72 g	0.3–1.2 g
Minerals										
Cations, total	4.1 mg. equiv	—		5.5 mg. equiv	—		6.8 mg. equiv	—	—	—
Sodium	15	2–44		29	19–54		48	26–136	58	31–214
Potassium	55	27–81		64	53–77		74	66–87	138	38–287
Calcium	33	15–61		34	18–63		31	13–66	125	56–381
Magnesium	4	2–6		4	2–5		4	1–8	13	7–22
Manganese	0.7 μg	—		—	—		trace	—	2 μg	<1–4 μg
Iron	0.15	0.02–0.45		0.04	0.02–0.05		0.09	0.02–>0.13	0.10	0.01–1.0
Copper	0.04	0.01–0.07		0.05	0.04–0.07		0.05	0.02–0.6	0.03	0.003–0.40
Anions, total	2.8 mg. equiv	—		3.7 mg. equiv	—		4.0 mg. equiv	—	—	—
Phosphorus	15	7–35		17	10–32		14	6–25	99	56–129
Sulphur	14	5–30		20	15–23		22	20–26	30	24–44
Chlorine	43	9–355		54	17–116		91	20–233	103	70–290
Total ions (ash) ...	6.9 mg. equiv	—		9.2 mg. equiv	—		10.8 mg. equiv	—	—	—
Alkaline excess ..	1.3 mg. equiv	—		1.8 mg. equiv	—		2.8 mg. equiv	—	—	—
Proteins, total ² ...	1200	1000–6000		1600	1000–3000		2700	1000–21,000	3300	2000–6000
Casein ²	400	40–700		700	400–1800		1200	300–5200	2800	1400–6300
Lactalbumin ² ...	300	100–600		800	—		—	—	400	200–600
Amino-acids, total ³	1280	900–1600		940	600–1000		1200	700–4000	3300	2700–4100
Arginine	43.3	27.8–	63.7 σ 8.8	62.8	47.7–	73.4 σ 6.9	74.4	62.0–	—	—
Histidine	23.7	12.4–	30.2 4.1	38.3	28.8–	44.9 4.6	41.2	34.9–	—	—
Isoleucine	61.0	40.9–	92.3 12.1	97.0	73.2–	120.9 11.0	101.1	88.2–	—	—
Leucine	96.6	65.3–	147.0 17.4	151.2	113.2–	197.0 21.9	165.6	133.4–	—	—
Lysine	70.1	36.2–	92.9 12.7	112.6	87.7–	148.4 15.7	117.7	95.0–	—	—
Methionine	11.6	6.5–	16.0 2.3	24.1	15.7–	34.4 4.0	25.3	18.6–	—	—
Phenylalanine ..	40.4	24.3–	57.8 6.9	62.4	48.4–	71.3 6.2	70.0	59.9–	—	—
Threonine	51.8	29.7–	65.6 8.5	78.1	60.6–	90.7 7.9	84.8	75.2–	—	—
Tryptophan	19.2	14.2–	26.0 3.0	28.2	23.0–	31.6 2.4	32.2	25.3–	—	—
Valine	72.5	44.7–	114.2 15.5	104.9	77.4–	136.0 12.2	116.9	97.8–	—	—
Non-protein										
nitrogen, total ...	32.4	17.3–	60.4 5.7	47.9	42.5–	53.3 —	—	—	—	13–14
Urea-N	18.0	12.7–	23.5 2.4	—	11.1	—	—	—	—	—
Uric acid-N	2.2	1.3–	4.1 0.5	—	—	—	—	—	—	—
Creatinine-N ...	1.1	0.8–	1.9 0.2	—	—	—	—	—	—	—
Creatine-N	1.1	0.2–	4.1 0.7	—	—	—	—	—	—	—
Amino-acid-N ..	5.0	2.8–	11.3 1.4	4.4	4.2–	4.7 —	—	—	—	—
Lactose										
(direct estimation)	7100	4900–	9500 400	6400	6100–	6700 —	—	—	—	—
(by difference) ...	6800	5000–	9200 600	6400	6000–	6800 —	—	—	—	—
Fats, total	3800	500–9000		3600	400–9600		2900	700–12,700	3700	900–9800
Fatty acids, essential	346	—		—	—		246	—	99	—
Vitamins										
Vitamin A, total ⁴	0.06	0.01–0.25		0.1	0.06–0.2		0.1	0.02–0.47	0.04	0.015–0.95
Vitamin B ₁	0.016	0.001–0.043		0.006	0–0.026		0.015	0.0005–0.082	0.042	0.031–0.090
Vitamin B ₂	0.043	0.013–0.100		0.033	0.027–0.049		0.030	0.012–0.050	0.157	0.020–0.342
Vitamin B ₁₂	trace	—		0.04 μg	trace–0.07 μg		0.04 μg	0.01–0.15 μg	0.56 μg	0.07–1.15 μg

¹) From ALBRITTON, E. C., *Standard Values in Nutrition and Metabolism*, Philadelphia, 1954; and MACY, I. G., *Amer. J. Dis. Child.*, **78**, 589, 1949.

²) Calculated by multiplying the appropriate N content by 6.37.

³) Total of available values.

⁴) Calculated from carotenoid content + preformed vitamin A.

	Mature milk (15 days to 20 months post partum)		Transitional milk (5–10 days post partum)		Colostrum (first 5 days post partum)		Cow's milk	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range
Vitamins (continued)								
Vitamin C	4.3	0–11.2	5.4	2.7–9.0	4.4	0.4–10.4	1.8	0.2–3.1
Vitamin D	0.4 I. U.	0–10 I.U.	–	–	–	–	2.4 I.U.	0.4–4 I.U.
Vitamin E	0.6	0.1–1	1.3	0.5–3	1.3	0.1–4	0.1	–
Nicotinic acid ¹ ..	0.172	0.066–0.69	0.175	0.06–0.36	0.075	<0.01–0.145	0.085	0.019–0.15
Pantothenic acid.	0.196	0.08–0.584	0.288	0.135–0.412	0.183	0.029–0.302	0.35	0.155–0.568
Pyridoxine	0.011	0.002–0.022	–	–	–	–	0.048	0.003–0.095
Biotin	0.0004	trace–0.0042	0.0004	trace–0.0018	0.0001	trace–0.0003	0.0035	0.0002–0.011
Folic acid	0.2 µg	0.1–50 µg	0.02 µg	0.015–0.025 µg	0.05 µg	0.01–0.15 µg	0.2 µg	0.1–5 µg
Inositol	39	19–56	–	–	–	–	13	3–39
Choline	9	5–14	–	–	–	–	13	4–28

¹) Nicotinic acid + nicotinamide.

Amino-acid composition of casein, whey and whole milk

(in milligrams per 100 ml of a sample of mature milk)

	Casein	Whey	Whole milk
Nitrogen	48.6	77.0	125.6
Histidine	6.0	6.3	12.3
Arginine	11.0	29.0	40.0
Lysine	17.3	32.4	49.7
Tyrosine	20.4	29.2	49.6
Tryptophan	5.7	13.0	18.7
Cystine	2.5	17.3	19.8
Methionine	7.2	10.9	18.1
Cystine-S	0.7	4.6	5.3
Methionine-S	1.5	2.3	3.8
Cystine-S + methionine-S	2.2	6.9	9.1

Fatty-acid composition of total milk fat

	Percentage by weight			Molar percentage		
	Mature milk	Colostrum		Mature milk	Colostrum	
		1st and 2nd day	3rd day		1st and 2nd day	3rd day
Saturated fatty acids						
Butyric acid	0.4	0.2	0.3	1.1	0.7	0.8
Caproic acid	0.1	0.1	0.1	0.1	0.3	0.2
Caprylic acid	0.3	0.8	0.1	0.6	1.5	0.1
Capric acid	2.2	3.5	0.9	3.3	5.3	1.4
Lauric acid	5.5	0.9	2.6	7.1	1.2	3.4
Myristic acid	8.5	2.8	4.9	9.6	3.3	5.7
Palmitic acid	23.2	24.6	27.8	23.4	25.4	28.9
Stearic acid	6.9	9.9	7.7	6.3	9.2	7.2
Remaining saturated fatty acids calculated as arachidic acid	1.1	4.9	2.7	0.9	4.1	2.3
Saturated fatty acids, total	48.2	47.7	47.1	52.4	51.0	50.0
Unsaturated fatty acids						
Decenoic acid	0.1	0.2	0.1	0.1	0.3	0.1
Dodecenoic acid	0.1	0.1	0.1	0.1	0.1	0.1
Tetradecenoic acid	0.6	0.1	0.2	0.7	0.1	0.2
Hexadecenoic acid	3.0	1.8	2.9	3.0	1.9	3.0
Oleic acid	36.5	36.0	37.1	33.3	33.8	35.1
Octadecadienoic acid	7.8	7.5	6.2	7.2	7.1	5.9
Octadecatrienoic acid	0.4	0.3	0.3	0.4	0.3	0.2
Eicosatetraenoic acid	0.9	1.8	1.6	0.8	1.5	1.4
Remaining unsaturated fatty acids calculated as eicosadienoic acid	2.4	4.6	4.7	2.0	3.9	4.0
Unsaturated fatty acids, total	51.8	52.4	53.2	47.6	49.0	50.0

	Content per 100 grams edible portion (unless otherwise stated)	Water g	Proteins g	Fats		Carbo- hydrates		Calories kcal	Vitamins					
				Total g	Choles- terol g	Total g	Fibre g		A* I.U.	B ₁ mg	B ₂ mg	Nicotinic acid mg	C mg	Other vitamins (vit. E in mg)
Fruit, Fruit juices														
1	Apples (sweet)													
	fresh	84.0	0.3	0.4	—	15.0	0.9	58	90	0.04	0.02	0.2	5	E 0.72
	per lb. as purchased	335	12	1.6	—	59.8	3.6	231	359	0.16	0.08	0.8	20	E 2.9
	1 apple, 2½" dia.	111	0.4	0.5	—	20	1.2	77	119	0.05	0.03	0.3	7	E 1.0
2	dried	20.0	3.0	0.7	—	73.6	4.0	281	0	0.05	0.08	0.5	11	—
3	Apple sauce, sweetened	79.8	0.2	0.1	—	19.7	0.6	80	80	0.01	0.01	trace	1	—
4	Apple juice, fresh	87	0.1	0	—	13	—	52	57	0.02	—	—	2	—
5	Apricots													
	fresh	85.3	0.9	0.2	—	12.9	1.0	51	2790	0.03	0.04	0.7	4	—
	per lb. as purchased	363	3.8	0.9	—	54.5	4.3	217	11,900	0.13	0.17	3.0	17	—
	1 apricot, medium	30	0.3	0.07	—	4.3	0.3	18	980	0.01	0.01	0.2	1.4	—
6	tinned, sweetened	77.3	0.6	0.1	—	21.4	0.4	89	1350	0.02	0.02	0.3	4	—
7	dried	24.0	5.2	0.4	—	66.9	2.6	292	7430	0.01	0.16	3.3	12	—
8	dried, cooked	67	1.3	0	—	31	0.7	129	2000	0.01	0.1	0.25	2	—
9	Bananas, fresh	73.5	1.3	0.4	—	24.0	0.5	94	430	0.09	0.06	0.6	10	E 0.37
	per lb. as purchased	223	3.9	1.2	—	73	1.5	285	1310	0.27	0.18	1.8	30	E 1.1
	1 banana, 6" = ca. 100 g													
10	Bilberries													
	fresh	83.4	0.6	0.6	—	15.1	1.2	68	280	0.03	0.07	0.3	16	—
11	tinned, sweetened	73	0.4	0.4	—	26	1.0	109	100	0.02	0.07	0.18	5	—
12	Blackberries													
	fresh	84	1.2	1.1	—	11.9	4.1	62	90	0.03	—	0.31	10	—
13	tinned, sweetened	79	0.7	0.7	—	19	2.5	85	50	0.01	0.03	0.18	3	—
14	Cherries													
	fresh	83.4	1.1	0.4	—	14.6	0.5	60	1000	0.05	0.06	0.14	8	—
	per lb. as purchased	355	4.7	1.7	—	62	2.1	255	4260	0.21	0.26	0.6	34	—
15	tinned, sweetened	78.1	0.6	0.1	—	20.8	—	235	870	0.03	0.02	0.18	3	—
16	candied	12	0.5	0.2	—	87	0.5	352	—	—	—	—	—	—
17	Currants, fresh	83.7	1.4	0.4	—	13.9	3.2	58	120	0.05	0.14	—	35	—
18	Dates, dried	20	2.2	0.6	—	75	2.4	314	180	0.08	0.05	2.18	0	—
19	Figs													
	fresh	71.7	1.2	0.4	—	16.1	1.4	65	75	0.09	0.08	0.63	2	—
20	dried	21.1	3.1	0.2	—	73.0	3.4	280	60	0.13	0.11	1.72	0	—
21	Gooseberries	89.9	0.8	0.5	—	8.3	1.2	37	380	0.15	—	—	25	—
22	Grapes	81.6	0.8	0.4	—	16.7	4.3	74	80	0.05	0.03	0.4	4	—
23	Grape juice	81	0.4	0	—	18	0	76	—	0.03	0.08	—	2	—
24	Grapefruit													
	fresh	89.0	0.6	0.2	—	9.8	0.5	39	trace	0.04	0.02	0.2	40	E 0.25; P
	per lb. as purchased	267	1.8	0.6	—	29	1.5	117	trace	0.12	0.06	0.6	120	E 0.75; P
	½ grapefruit, 4¼" dia. .	167	1.1	0.4	—	18.4	0.9	73	trace	0.08	0.04	0.4	75	E 0.5; P
25	tinned, sweetened	79.8	0.6	0.2	—	19.1	0.3	81	trace	0.03	0.02	0.2	30	—
26	Grapefruit juice, fresh	89.4	0.4	0.1	—	10	—	42	trace	0.04	0.02	0.2	45	P
27	Lemon juice	89.3	0.9	0.6	—	8.7	—	45	0	0.04	trace	0.1	45	P
28	Oranges, fresh	87.1	0.9	0.2	—	11.3	0.8	45	190	0.08	0.03	0.2	49	E 0.23; B ₆ ; P
	per lb. as purchased	284	2.9	0.7	—	37	2.6	147	620	0.26	0.10	0.7	160	E 0.75; B ₆ ; P
	1 orange, 3" dia.	135	1.4	0.3	—	17.5	1.2	70	290	0.12	0.05	0.3	76	E 0.4; B ₆ ; P
29	Orange juice, fresh	86	0.6	0.1	—	12.9	0	49	100	0.07	0.02	0.2	42	B ₆ ; P

* A = vitamin-A activity due to carotenes; 1 I.U. vitamin A = 0.0006 mg β-carotene.

	Other organic constituents					Excess acid as N-HCl	Excess base as N-NaOH	Minerals									
	Malic acid	Citric acid	Oxalic acid	Uric acid	Purine bases			Sodium	Potassium	Calcium	Magne- sium	Manga- nese	Iron	Copper	Phospho- rus	Sulphur	Chlorine
	mg	mg	mg	mg	mg	ml	ml	Na mg	K mg	Ca mg	Mg mg	Mn mg	Fe mg	Cu mg	P mg	S mg	Cl mg
1	270	0	0	0	0	0	3.4	2	116	6	6	0.084	0.3	0.071	10	5	4
	1080	0	0	0	0	0	13.6	8	462	24	24	0.34	1.2	0.28	40	20	16
	356	0	0	0	0	0	4.5	2.6	153	8	8	0.11	0.4	0.093	13	7	5
2	—	0	0	0	0	0	+	—	—	24	—	—	4.1	—	42	—	—
3	—	—	0	0	0	0	+	0.3	55	4	—	—	0.2	—	6	—	—
4	—	—	0	0	0	0	+	4	100	—	—	—	—	—	—	—	—
5	—	—	14	0	0	0	6.8	0.6	440	16	9	—	0.5	—	23	6	2
	—	—	60	0	0	0	29	2.6	1875	68	38	—	2.1	—	98	26	9
	—	—	4.9	0	0	0	2.4	0.2	154	5	3	—	0.2	—	8	2	1
6	330	1060	trace	0	0	0	+	2	65	10	—	—	0.3	—	15	—	—
7	810	350	trace	0	0	0	61	11	1700	86	—	—	4.9	—	119	—	—
8	—	—	—	0	0	0	+	—	—	10	—	—	0.3	—	15	—	—
9	500	150	6.4	0	0	0	5.6	0.5	420	8	31	0.642	0.6	0.20	28	12	125
	1520	455	19	0	0	0	17	1.5	1275	24	94	1.95	1.8	0.61	85	36	380
10	100	1560	15	0	0	0	2.7	0.5	65	16	10	—	0.8	—	13	11	8
	—	—	—	0	0	0	+	—	—	10	—	—	0.5	—	10	—	—
12	160	trace	18	0	0	0	5.5	4	181	17	24	—	1.0	—	34	17	15
	—	—	—	0	0	0	+	—	—	15	—	—	0.7	—	30	—	—
14	1250	10	0	0	0	0	6.1	1	260	19	14	—	0.5	—	31	8	3
	5320	43	0	0	0	0	26.0	4	1110	81	60	—	2.1	—	132	34	13
15	—	—	0	0	0	0	+	0.7	77	11	—	—	0.3	—	14	—	—
16	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
17	50	2300	19	0	0	0	1.2	2	261	26	15	—	0.7	—	38	29	13
18	—	—	—	0	0	0	11	0.9	790	65	65	—	5.1	—	72	65	283
19	trace	340	—	0	0	0	++	2	190	50	21	—	0.8	—	40	12	16
	—	—	—	0	0	0	100	34	780	162	82	—	4.0	—	116	69	105
21	1400	+	88	0	0	0	7.3	1	149	35	9	—	4.7	—	31	15	9
22	650	—	0	0	0	0	3.1	2	254	17	7	0.083	0.6	0.098	21	9	2
23	310	20	0	0	0	0	3.9	1	120	10	—	—	0.3	—	10	—	—
24	—	1460	0	0	0	0	4.2	0.5	198	17	10	—	0.3	—	18	8	3
	—	4380	0	0	0	0	12.6	1.5	594	51	30	—	0.9	—	54	24	9
	—	2750	0	0	0	0	7.9	0.9	372	32	19	—	0.6	—	34	15	6
25	—	—	0	0	0	0	+	0.4	150	13	—	—	0.3	—	14	—	—
26	—	—	0	0	0	0	+	139	139	8	8	—	0.4	—	7	5	2
27	290	6080	0	0	0	0	4.1	2	148	14	9	—	0.1	—	10	8	4
28	trace	980	24	0	0	0	5.6	0.3	170	33	10	0.025	0.4	0.076	23	8	4
	trace	3200	78	0	0	0	18.3	1.0	555	108	33	0.08	1.3	0.25	75	26	13
	trace	1520	37	0	0	0	8.7	0.5	260	51	15	0.04	0.6	0.12	35	12	6
29	—	—	—	0	0	0	6.5	0.5	190	33	10	0.025	0.4	0.076	23	8	4

	Content per 100 grams edible portion (unless otherwise stated)	Water g	Proteins g	Fats		Carbo- hydrates		Calories kcal	Vitamins						
				Total g	Choles- terol g	Total g	Fibre g		A* I.U.	B ₁ mg	B ₂ mg	Nicotinic acid mg	C mg	Other vitamins (vit. E in mg)	
30	Peaches														
	fresh	86.6	0.8	0.2	—	11.8	0.6	47	880	0.02	0.05	0.9	8	—	
	<i>per lb. as purchased</i>	762	3.2	0.8	—	47	2.4	188	3520	0.08	0.20	3.6	32	—	
	<i>1 peach, 2½" dia. =</i> <i>ca. 100 g</i>														
31	tinned, sweetened	80.9	0.4	0.1	—	18.2	0.2	75	450	0.01	0.02	0.7	4	—	
32	dried	24	3.0	0.6	—	69.4	3.5	295	3250	0.01	0.20	5.4	19	—	
33	Pears														
	fresh	83.2	0.5	0.4	—	15.5	1.5	61	20	0.02	0.04	0.1	4	—	
	<i>per lb. as purchased</i>	313	1.9	1.5	—	58	5.6	230	75	0.08	0.15	0.4	15	—	
	<i>1 pear, 2½" dia.</i>	125	0.8	0.6	—	23.4	2.3	92	30	0.03	0.06	0.2	6	—	
34	tinned, sweetened	81.1	0.2	0.1	—	18.4	1.5	75	trace	0.01	0.02	0.1	2	—	
35	dried	24	2.3	0.4	—	72	6.1	301	45	0.07	0.15	—	0	—	
36	Pineapple														
	fresh	86.7	0.4	0.2	—	12.2	0.5	47	130	0.03	0.02	0.2	24	—	
	tinned, sweetened	78.0	0.4	0.1	—	21.1	0.3	87	80	0.07	0.02	0.2	9	—	
38	Pineapple juice, tinned	86.2	0.3	0.1	—	13.0	—	54	80	0.05	0.02	0.2	9	—	
39	Plums														
	fresh	85.7	0.7	0.2	—	12.9	0.5	56	350	0.15	0.03	0.6	5	—	
	<i>per lb. as purchased</i>	369	3.0	0.9	—	56	2.2	241	1510	0.65	0.13	2.6	22	—	
	<i>1 plum, 2" dia.</i>	49	0.4	0.1	—	7.4	0.3	32	200	0.09	0.02	0.3	3	—	
40	tinned, sweetened	78.6	0.4	0.1	—	20.4	0.3	84	230	0.03	0.03	0.4	1	—	
41	dried	24.0	2.3	0.6	—	71.0	1.6	299	1890	0.10	0.16	1.7	3	—	
42	Raisins	24	2.3	0.5	—	71.2	1.8	298	50	0.15	0.08	0.5	trace	—	
43	Raspberries														
	fresh	83	1.1	0.6	—	14.4	2.8	66	150	0.03	—	—	25	—	
	tinned, sweetened	71	0.6	0.5	—	28	1.9	119	100	0.02	—	—	—	—	
45	Raspberry juice, fresh	88	0.2	0	—	11	—	45	100	0.03	—	—	25	—	
46	Strawberries														
	fresh	90	0.8	0.6	—	8.1	1.2	41	60	0.03	0.07	0.3	60	—	
	tinned, sweetened	71	0.5	0.2	—	28	0.7	116	—	—	—	—	—	—	
48	Water melons														
	fresh	92.1	0.5	0.2	—	6.9	0.6	31	590	0.05	0.05	0.2	6	—	
	<i>per lb. as purchased</i>	192	1.0	0.4	—	14	1.3	65	1230	0.10	0.10	0.4	13	—	
Vegetables															
49	Artichokes, fresh	83.7	3.0	0.2	—	11.8	1.9	51	200	0.08	0.03	—	9	—	
50	Asparagus														
	fresh	92.9	2.1	0.2	—	4.1	0.8	21	800	0.12	0.17	1.2	36	—	
	tinned	93.6	1.6	0.3	—	3.0	0.5	21	600	0.06	0.09	0.8	15	—	
52	Beans (green)														
	fresh	89.1	2.4	0.2	—	7.6	1.5	35	700	0.06	0.12	0.6	12	E 3.6	
	tinned	94	1.0	0	—	3.8	0.6	19	410	0.03	0.05	0.3	4	—	
54	Beetroots	87.6	1.6	0.1	—	9.6	0.9	33	6	0.03	0.04	0.3	5.5	E	
55	Brussels sprouts	84.8	4.7	0.5	—	8.7	1.2	47	50	0.09	0.1	0.5	68	K	
56	Cabbage														
	fresh	91.8	1.6	0.1	—	5.7	1.0	25	100	0.06	0.05	0.26	40-70**	E 0.1; K++	
	dried	8.8	13.7	1.8	—	68.8	—	346	520	0.41	0.37	2.4	189	K+++	
58	Carrots														
	fresh	88.6	1.1	0.2	—	9.1	1.0	40	6000	0.13	0.06	0.64	4	E 0.45	
	<i>1 carrot, 6"</i>	44	0.5	0.1	—	4.5	0.5	20	3000	0.06	0.03	0.3	2	E 0.2	
59	tinned	92.2	0.5	0.4	—	6.1	0.6	30	4500	0.03	0.02	0.3	2	—	
60	dried	5.6	4.0	1.4	—	83.1	—	361	60,000	0.29	0.28	3.2	11	—	
61	Cauliflower	91.7	2.4	0.2	—	4.9	0.9	31	90	0.10	0.11	0.6	69	E	

* A = vitamin-A activity due to carotenes; 1 I.U. vitamin A = 0.0006 mg β-carotene.

** The interior is richer in vitamin C.

	Other organic constituents					Minerals											
	Malic acid	Citric acid	Oxalic acid	Uric acid	Purine bases	Excess acid as N-HCl	Excess base as N-NaOH	Sodium	Potassium	Calcium	Magne-sium	Manga-nese	Iron	Copper	Phospho-rus	Sulphur	Chlorine
	mg	mg	mg	mg	mg	ml	ml	Na mg	K mg	Ca mg	Mg mg	Mn mg	Fe mg	Cu mg	P mg	S mg	Cl mg
30	370	370	trace	0	0	0	5.0	0.5	160	8	11	—	0.6	—	22	7	5
	1480	1480	trace	0	0	0	20.0	2.0	640	32	44	—	2.4	—	88	28	20
31	690	50	trace	0	0	0	4.5	5	31	5	—	—	0.4	—	14	—	—
32	—	—	—	0	0	0	+	12	1100	44	—	—	6.9	—	126	—	—
33	120	240	3	0	0	0	3.6	3	129	13	9	0.064	0.3	0.134	16	7	4
	452	903	11	0	0	0	13.6	11.3	485	49	34	0.24	1.1	0.50	60	26	15
	180	360	5	0	0	0	5.4	4.5	195	20	14	0.10	0.5	0.22	24	11	6
34	—	—	—	0	0	0	1.5	8	52	8	—	—	0.2	—	10	—	—
35	—	—	—	0	0	0	+	—	—	30	—	—	5.4	—	165	—	—
36	—	—	—	0	0	0	6.8	0.3	210	16	11	—	0.3	—	11	7	46
37	120	840	6.3	0	0	0	+	1	120	29	—	—	0.6	—	7	—	—
38	—	—	—	0	0	0	+	0.5	140	15	—	—	0.5	—	8	—	—
39	920	30	10	0	0	+	0	0.6	170	17	11	0.096	0.5	0.080	20	5	2
	3960	129	43	0	0	+	0	2.6	732	73	47	0.41	2.2	0.34	86	22	9
	530	17	6	0	0	+	0	0.3	97	10	6	0.06	0.3	0.046	11	3	1
40	—	—	—	0	0	+	0	18	110	8	—	—	0.3	—	12	—	—
41	—	—	—	0	0	+	0	5	848	54	40	—	3.9	—	85	28	9
42	—	—	0	0	0	0	23.7	31	708	78	35	—	3.3	—	129	42	45
43	40	1300	—	0	0	0	6.7	3	190	49	23	—	1.0	—	52	18	22
44	—	—	—	0	0	0	+	—	—	20	—	—	0.5	—	20	—	—
45	—	—	—	0	0	0	+	5	134	20	16	—	—	—	10	9	—
46	160	1080	19	0	0	0	6.6	2	145	28	12	0.219	0.8	0.075	27	12	11
47	—	—	—	0	0	0	+	—	—	—	—	—	—	—	—	—	—
48	—	—	0	0	0	0	2.7	0.3	121	7	10	—	0.2	—	12	9	8
	—	—	0	0	0	0	5.6	0.6	252	15	21	—	0.4	—	25	19	17
49	170	100	—	+	—	0	+	43	430	40	27	—	1.0	—	90	20	57
50	100	110	5.2	24	8	0	0.8	2	240	23	12	0.190	0.9	0.141	60	46	36
51	—	—	+	+	+	0	+	410	130	20	—	—	1.0	—	34	—	—
52	130	30	31	6	2	0	5.4	0.9	300	73	26	0.326	1.2	0.126	44	30	33
53	—	—	—	+	+	0	+	410	120	27	—	—	1.4	—	19	—	—
54	—	—	338	—	—	0	10.8	110	350	30	23	0.577	1.0	0.187	37	17	61
55	200	240	5.9	0	0	0	7.0	24	400	26	—	—	1.0	—	50	184	—
56	100	140	7.3	6	2	0	4.5	18	294	43	12	0.114	0.6	0.099	23	67	39
57	—	—	—	+	+	0	+	—	—	374	—	—	4.7	—	274	—	—
58	240	90	33	0	2	0	10.8	48	311	41	17	0.247	0.9	0.111	34	21	42
	120	45	16	0	1	0	5.4	24	155	20	8	0.12	0.4	0.06	17	10	21
59	—	—	—	0	(+)	0	+	280	110	22	—	—	0.6	—	24	—	—
60	—	—	—	0	(+)	0	+	—	—	242	—	—	5.9	—	102	—	—
61	390	210	0	24	8	0	5.3	24	400	22	—	—	1.1	—	72	—	—

Content per 100 grams edible portion (unless otherwise stated)		Water		Proteins		Fats		Carbo- hydrates		Calories		Vitamins					
												A*	B ₁	B ₂	Nicotinic acid	C	Other vitamins
		g	g	g	g	g	g	g	g	kcal		I.U.	mg	mg	mg	mg	(vit. E in mg)
62	Celery leaves	93.3	1.1	0.2	—	4.3	0.9	20	0	0.03	0.04	0.3	7	E 0.46			
63	stalk, bleached	93.7	1.3	0.2	—	3.7	0.7	18	0	0.05	0.04	0.4	7	—			
64	Chicory and endives	93.1	1.7	0.2	—	4.1	0.9	20	3600	0.10	0.20	0.72	14	K			
65	Cucumbers	95.6	0.8	0.1	—	3.0	0.6	13	200	0.04	0.05	0.18	10	B ₆ ; E			
	1 cucumber, 7 ¹ / ₂ " × 2" ...	277	2.3	0.3	—	8.7	1.7	28	580	0.12	0.14	0.5	29	B ₆ ; E			
66	Dandelion leaves	85.8	2.7	0.7	—	8.8	0.7	52	13,650	0.19	0.14	0.8	36	K			
	Haricot beans																
67	dried	10.5	22.0	1.5	—	62.1	4.4	350	0	0.60	0.24	2.1	2	E			
68	tinned	74	6.0	0.4	—	19	1.0	102	0	0.13	0.12	0.88	0	—			
	Kohlrabi																
69	leaves	89.3	3.1	0.4	—	5.4	1.2	30	9540	0.10	0.56	0.8	136	E 2.2			
70	tubers	90.5	2.1	0.2	—	6.2	1.1	29	trace	0.06	0.06	0.5	28	—			
71	Lentils, dried	10	25.7	1.0	—	59.2	2.0	357	50	0.5	0.32	3.10	0	E++			
72	Lettuce	94.8	1.3	0.2	—	2.8	0.6	15	540	0.06	0.07	0.2	8	E 0.45			
73	young	94.8	1.2	0.2	—	2.9	0.7	18	1620	0.06	0.07	0.2	18	E			
	Onions (mature)																
74	fresh	88.8	1.4	0.2	—	9.0	0.8	40	50	0.03	0.02	0.1	12	E 0.27			
	1 onion, 2 ¹ / ₂ " dia.	98	1.5	0.2	—	9.9	0.9	44	55	0.03	0.02	0.1	13	E 0.3			
75	dried	9.9	10.1	1.0	—	75.2	—	350	20	0.23	0.15	1.1	37	—			
76	Parsley	84	3.7	1.0	—	9	1.8	60	18,000	—	—	—	189	E; K			
	Parsnips																
77	raw	78.6	1.5	0.5	—	18.2	2.2	78	0	0.08	0.12	0.2	18	—			
78	cooked	83.5	1.0	0.5	—	13.9	2.1	60	0	0.06	0.10	0.2	12	—			
	Peas																
79	fresh	75.0	6.7	0.4	—	17.0	0.2	80	690	0.30	0.18	1.9	26	B ₆ ; E 2.1			
80	tinned	82.3	3.4	0.4	—	12.9	1.3	69	540	0.11	0.06	0.9	8	—			
81	dried	10.0	24.5	1.0	—	61.7	4.4	354	370	0.87	0.29	3.0	2	E+			
82	Peppers, green	92.8	1.2	0.2	—	5.3	1.4	24	630	0.07	0.04	0.4	120	—			
	Potatoes																
83	fresh	77.8	2.0	0.1	—	19.1	0.4	85	40	0.10	0.04	1.0	23	E 0.06			
	per lb. as purchased	272	7.0	0.4	—	67	1.4	297	140	0.35	0.14	3.5	80	E 0.2			
84	dried	7.2	7.1	0.7	—	82.0	—	363	400	0.25	0.10	4.8	26	—			
85	Pumpkins	95.0	0.8	0.1	—	3.5	0.6	15	3400	0.05	0.08	0.6	8	—			
86	Radishes	93.7	1.1	0.1	—	4.2	0.7	20	30	0.04	0.04	0.1	24	—			
87	Rhubarb	94.9	0.5	0.1	—	3.8	0.7	18	30	0.01	—	0.1	9	—			
88	Sauerkraut	93.2	1.1	0.2	—	3.4	1.4	20	trace	0.03	0.20	0.2	18	—			
89	Soya beans, dried	7.5	34.9	18.1	—	12.0	4.4	351	110	1.14	0.31	2.1	trace	E, pant. a.			
	Spinach																
90	fresh	92.1	2.2	0.3	—	3.9	0.7	22	6000	0.08	0.2	0.5	21.5	E			
91	tinned	92.3	2.3	0.4	—	3.0	0.6	22	5800	0.02	0.08	0.3	5	—			
	Tomatoes																
92	fresh	94.1	1.0	0.3	—	4.0	0.6	23	1100	0.06	0.04	0.6	23	E 0.27; K			
	1 tomato, 2 ¹ / ₂ " dia.	141	1.5	0.4	—	6.0	0.9	34	1650	0.09	0.06	0.9	34	E 0.4; K			
93	tinned	94.2	1.0	0.2	—	3.9	0.5	21	1050	0.05	0.03	0.7	16	—			
94	Tomato ketchup	69.5	2.0	0.4	—	24.5	—	217	1880	0.09	0.07	1.8	28	—			
95	Tomato juice, tinned	93.5	1.0	0.2	—	4.3	0	23	1050	0.05	0.03	0.7	16	—			
	Turnips																
96	raw	90.9	1.1	0.2	—	7.1	1.1	32	trace	0.05	0.07	0.5	28	—			
97	cooked	92.3	0.8	0.2	—	6.0	1.2	27	trace	0.04	0.06	0.4	18	—			

* A = vitamin-A activity due to carotenes; 1 I. U. vitamin A = 0.0006 mg β-carotene.

	Other organic constituents					Excess acid as N-HCl	Excess base as N-NaOH	Minerals									
	Malic acid	Citric acid	Oxalic acid	Uric acid	Purine bases			Sodium	Potassium	Calcium	Magne- sium	Manga- nese	Iron	Copper	Phospho- rus	Sulphur	Chlorine
	mg	mg	mg	mg	mg	ml	ml	Na mg	K mg	Ca mg	Mg mg	Mn mg	Fe mg	Cu mg	P mg	S mg	Cl mg
62	170	10	50	15	5	0	7.8	96	291	50	27	—	0.5	—	40	22	137
63	—	—	—	—	—	—	—	—	—	50	—	—	0.5	—	40	—	—
64	—	—	27.3	+	+	0	4.8	18	400	104	13	—	—	—	38	32	71
65	—	—	0	0	0	0	7.9	0.8	140	10	9	—	0.3	—	21	12	30
	—	—	0	0	0	0	22.9	2.3	410	29	26	—	0.9	—	61	35	87
66	—	—	24.6	+	+	0	19.5	76	430	187	36	—	3.1	—	70	170	99
67	—	—	—	++	++	0	12.4	0.3	1201	148	159	0.957	10.3	1.503	463	237	35
68	—	—	—	+	+	0	3.0	310	210	60	—	—	2.1	—	190	—	—
69	—	—	+	+	+	0	+	10	440	259	19	—	1.5	—	50	54	92
70	230	0	1.8	33	11	0	8.5	37	230	40	16	0.083	0.5	0.085	34	58	52
71	—	—	—	162	54	+	0	3	1200	107	86	—	8.6	—	438	277	60
72	170	20	7.1	9	3	0	7.4	12	140	22	11	0.777	0.5	0.069	25	18	73
73	—	—	+	+	+	0	+	—	—	62	—	—	1.1	—	20	—	—
74	170	20	23	0	0	0	1.5	1	130	32	15	0.363	0.5	0.130	44	68	24
	187	22	25	0	0	0	1.6	1	140	35	16	0.39	0.5	0.14	48	75	26
75	—	—	—	0	0	0	+	—	—	158	—	—	3.1	—	256	—	—
76	—	—	190	+	+	0	+	28	880	190	—	—	3.2	—	80	—	—
77	—	—	—	—	—	—	—	—	—	57	—	—	0.7	—	80	—	—
78	—	—	—	—	—	—	—	—	—	57	—	—	0.7	—	80	—	—
79	80	110	0	54	18	0	1.3	0.9	380	22	27	—	2.0	—	118	56	33
80	—	—	0	+	+	0	+	270	96	25	—	—	1.8	—	67	—	—
81	—	—	0	++	++	0	+	42	880	73	140	1.99	6.0	0.802	397	196	44
82	—	—	16	+	+	0	1.7	0.5	186	11	12	0.126	0.4	0.107	25	19	19
83	0	510	5.7	0	1	0	7.0	0.8	410	14	27	0.173	0.8	0.164	52	29	35
	0	1780	20	0	3.5	0	24.4	2.8	1430	49	94	0.60	2.8	0.57	182	101	122
84	0	—	—	0	(+)	0	+	—	—	25	—	—	3.7	—	103	—	—
85	—	—	—	0	0	0	1.5	1	457	21	12	—	0.8	—	44	13	49
86	—	—	0	15	5	0	2.9	8	229	37	15	—	1.0	—	31	31	37
87	1770	410	500	—	—	—	—	2	358	51	16	—	0.5	—	25	8	53
88	—	—	—	+	+	0	5.5	730	490	46	—	—	0.5	—	31	—	—
89	—	—	—	+	+	0	+	4	1900	227	—	—	8.0	—	586	—	—
90	90	80	892	72	24	0	27.0	84	489	87	55	0.828	3.0	0.197	45	27	65
91	—	—	+++	++	+	0	+	300	260	90	—	—	1.6	—	33	—	—
92	150	390	7.5	—	—	0	5.5	4	268	11	12	0.189	0.6	0.097	27	14	40
	225	585	11	—	—	0	8.2	6	400	16	18	0.28	0.9	0.15	40	21	60
93	—	—	—	—	—	0	+	18	130	11	—	—	0.6	—	27	—	—
94	—	—	—	—	—	0	+	1300	800	40	—	—	2.0	—	54	—	—
95	—	—	—	—	—	0	+	230	230	7	10	—	0.4	—	15	5	55
96	—	—	—	—	—	—	—	—	—	40	—	—	0.5	—	34	—	—
97	—	—	—	—	—	—	—	—	—	40	—	—	0.5	—	34	—	—

	Content per 100 grams edible portion (unless otherwise stated)	Water g	Proteins g	Fats		Carbo- hydrates		Calories kcal	Vitamins					
				Total g	Choles- terol g	Total g	Fibre g		A* I.U.	B ₁ mg	B ₂ mg	Nicotinic acid mg	C mg	Other vitamins (vit. E in mg)
98	Turnip tops	90.4	2.0	0.3	—	5.6	1.4	33	6700	0.05	0.17	0.3	34	E
99	Watercress	95	0.7	0.5	—	3.7	0.5	22	4000	0.10	0.27	—	75	—
Nuts														
100	Almonds	4.7	18.6	54.1	—	19.6	2.0	640	0	0.25	0.67	4.6	trace	—
101	Brazil nuts	5	14.4	65.9	—	11	2.1	695	10	0.50	—	—	—	—
Chestnuts														
102	fresh	48	3.4	1.9	—	45.6	1.3	213	80	0.23	—	1.17	6	—
103	dried	9	6.7	4.1	—	79	2.5	380	—	—	—	—	—	—
Coconuts														
104	fresh	48	4.2	34.0	—	12.8	3.3	351	—	0.09	—	0.40	2	—
105	dried	3.3	3.6	39.1	—	53.2	4.1	579	0	0.03	trace	trace	0	—
106	Groundnuts, roasted	5.2	25.9	43.3	—	23.4	3.3	546	0	0.30	0.16	16.2	0	B ₆ ; pant. a.
107	Hazel nuts	6	12.7	60.9	—	18	3.4	671	100	0.40	—	—	3	—
108	Walnuts	3.3	15.0	64.4	—	15.6	2.1	702	30	0.48	0.13	1.2	3	P
Bread, Flour, Cereal products														
Bread														
109	brown, unenriched	37	8.9	1.8	—	52.1	1.1	266	0	0.30	0.13	3.54	0	E++
110	rye-	37.6	6.4	3.4	—	51.7	0.5	263	0	0.16	0.04	1.1	0	—
111	white, unenriched	36	8.5	2.0	—	52	—	260	0	0.24	0.15	2.2	0	E 0.23
112	toasted	26	9.7	2.3	—	59	—	296	0	0.25	0.17	2.5	—	—
113	wholemeal	37	9.5	3.5	—	48.0	1.2	262	0	0.28	0.15	3.5	0	B ₆ ; E 1.3
Flour														
114	buckwheat	12	6.3	1.1	—	79.7	—	354	0	0.31	0.08	2.1	0	—
115	rice	12	7.4	0.5	—	80	0.4	354	0	0.04	—	0.1–0.3	0	E 0.35
116	rye	12	11.0	1.9	—	73.1	—	319	0	0.47	0.21	1.7	0	—
117	soya, full fat	9	35.9	20.6	—	11.4	—	375	140	0.77	0.28	0.3	0	—
118	medium defatted ...	9	42.5	6.5	—	13.6	—	283	110	0.82	0.34	0.25	0	—
119	starch	12	0.5	0.3	—	86.9	0.2	362	0	0	0	0	0	0
120	wheat, white	12	10.8	1.1	—	75.5	0.3	370	0	0.07	0.03	0.06–0.08	0	E 1.2
121	whole	12	12.2	2.3	—	71.8	2.1	334	0	0.56	0.12	0.4–0.6	0	E 2.2
Maize														
122	groats	12	8.3	1.2	—	78.0	—	356	300	0.15	0.06	0.9	0	—
123	cornflakes	9.3	7.9	0.7	—	80.3	0.2	359	0	0.16	0.08	1.6	0	—
124	Oat flakes	10.0	13.0	7.5	—	67.8	1.9	385	0	0.55	0.14	1.1	0	E 1.9; pant. a.
125	cooked	85	2.8	0.5	—	11.5	0.2	62	0	—	—	—	0	—
Pastry														
126	egg-	9.1	14.3	5.0	—	70.6	0.3	385	200	0.13	0.12	2.1	0	0
127	ordinary, dried	11	13	1.4	—	73.9	0.4	360	0	0.13	0.08	2.1	0	0
128	cooked	83	2.5	0.2	—	14.2	0.1	69	0	0.03	0.02	0.60	0	0
129	Pearl barley	12.0	9.0	1.4	—	76.5	0.8	346	0	0.12	0.08	3.1	0	—
Rice														
130	polished	12.3	7.6	0.3	—	79.4	0.2	351	0	0.05	0.03	1.4	0	0
131	polished, cooked	74	2.2	0.1	—	22.5	0.1	100	0	—	—	—	—	—
132	whole	12.0	7.5	1.7	—	77.7	0.6	356	0	0.29	0.05	4.6	0	E
133	bran	9	11.6	10.1	—	64	2.2	393	—	2.20	0.23	96.6	0	E++
134	Tapioca	12.6	0.6	0.2	—	86.4	0.1	350	0	—	0.10	—	0	0
135	Wheat germ	11.0	25.2	10.0	—	49.5	2.5	389	0	2.05	0.80	4.6	0	E+++ ¹⁾

* A = vitamin-A activity due to carotenes; 1 I.U. vitamin A = 0.0006 mg β-carotene.

¹⁾ Wheat-germ oil: vitamin-E content = 150–250 mg/100 g.

	Other organic constituents					Excess acid as N-HCl ml	Excess base as N-NaOH ml	Minerals										
	Malic acid	Citric acid	Oxalic acid	Uric acid	Purine bases			Sodium	Potassium	Calcium	Magne- sium	Manga- nese	Iron	Copper	Phospho- rus	Sulphur	Chlorine	
	mg	mg	mg	mg	mg			Na mg	K mg	Ca mg	Mg mg	Mn mg	Fe mg	Cu mg	P mg	S mg	Cl mg	
98	—	—	916	—	—	0	27.0	130	570	118	—	—	3.2	—	45	—	—	
99	—	—	—	+	+	0	+	—	301	187	28	—	7.2	—	5	147	109	
100	—	—	—	—	—	0	12.1	3	690	254	252	—	4.4	—	475	150	20	
101	—	—	—	—	—	0	13.0	16	601	120	225	—	2.8	—	600	198	81	
102	—	—	—	—	—	0	7.4	7	410	30	42	—	0.7	—	90	48	11	
103	—	—	—	—	—	0	+	—	—	—	—	—	—	—	—	—	—	
104	—	—	—	—	—	0	+	39	363	20	39	—	2.7	—	100	32	122	
105	—	—	—	—	—	0	+	53	693	43	77	—	3.6	—	191	76	225	
106	—	—	—	—	—	3.9	0	2	740	74	167	—	1.9	—	393	226	41	
107	—	—	—	—	—	+	0	19	618	290	140	—	4.1	—	350	198	67	
108	—	—	—	—	—	7.9	0	2	450	83	134	—	2.1	—	380	146	36	
109	0	0	0	0	0	7.5	0	—	—	50	—	—	2.5	—	218	—	—	
110	0	0	0	0	0	6.8	0	560	100	22	—	—	0.8	—	96	—	—	
111	0	0	0	0	0	7.1	0	446	109	30	30	0.310	0.8	0.205	110	54	621	
112	—	—	—	—	—	8.2	0	516	126	35	35	0.36	0.9	0.24	127	62	718	
113	0	0	0	0	0	7.3	0	430	450	60	150	—	2.6	—	370	150	—	
114	0	0	0	0	0	+	0	1	130	11	48	—	1.0	—	88	71	12	
115	0	0	0	0	0	+	0	—	79	10	28	—	0.9	—	100	—	6	
116	0	0	0	0	0	+	0	61	450	61	155	3.067	4.8	0.656	369	146	40	
117	0	0	0	++	++	+	0	—	—	195	223	—	12.1	—	553	300	24	
118	0	0	0	++	++	+	0	0.6	1700	244	—	—	13.0	—	610	—	—	
119	0	0	0	0	0	+	0	4	4	trace	—	—	trace	—	trace	—	—	
120	0	0	0	0	0	11.5	0	1	130	19	21	0.713	0.7	0.147	93	109	71	
121	0	0	0	0	0	+	0	—	324	38	122	4.280	2.3	0.435	385	124	177	
122	0	0	0	0	0	+	0	0.6	213	10	84	—	0.2	—	140	111	146	
123	0	0	0	0	0	5.4	0	660	160	10	—	—	1.0	—	56	—	—	
124	0	0	0	0	0	12.9	0	2	340	54	145	4.945	5.2	0.738	365	199	49	
125	0	0	0	0	0	+	0	—	—	11	—	—	0.6	—	65	—	—	
126	0	0	0	—	—	+	0	—	—	24	—	—	1.9	—	156	—	—	
127	0	0	0	0	0	10.5	0	12	174	22	34	—	1.2	—	144	146	52	
128	0	0	0	0	0	+	0	—	—	4	—	—	0.2	—	25	—	—	
129	0	0	0	0	0	10.5	0	3	160	16	37	1.684	2.0	0.753	189	116	—	
130	0	0	0	0	0	11.0	0	2	79	9	28	1.014	0.7	0.183	92	—	6	
131	0	0	0	0	+	+	0	—	—	2	—	—	0.2	—	24	—	—	
132	0	0	0	0	4	+	0	—	342	39	119	—	5.5	—	303	—	23	
133	0	0	0	—	—	+	0	—	—	60	—	—	16.0	—	1450	—	—	
134	0	0	0	0	0	0	0	4	20	12	2	—	1.0	—	12	4	16	
135	0	0	0	—	—	+	0	2	780	84	—	—	8.1	—	1096	—	—	

	Content per 100 grams edible portion (unless otherwise stated)	Water	Proteins	Fats		Carbo-hydrates		Calories	Vitamins					
				Total	Choles-terol	Total	Fibre		A*	B ₁	B ₂	Nicotinic acid	C	Other vitamins
		g	g	g	g	g	g	kcal	I.U.	mg	mg	mg	mg	(vit. E in mg)
Sugar, Confectionery														
136	Cane sugar raw	3	0	0	—	96	0	384	0	0	0	0	0	0
137	refined	0	0	0	—	100	0	387	0	0	0	0	0	0
138	Caramel	7	2.0	12.0	—	78	0	428	—	—	—	—	—	—
Chocolate														
139	plain	2.3	5.5	52.9	—	18	—	570	0	trace	0.24	1.1	0	E 5.3; biotin
140	milk	1	6.0	33.5	—	54	0	542	183	0.02	0.04	0.33	0	biotin
141	Glucose	0	0	0	—	100	0	387	0	0	0	0	0	0
142	Honey	20-21	0.3	0	—	79.5	0	319	0	trace	0.04	0.2	4	—
143	Jams	28.0	0.5	9.3	—	70.8	0	288	10	0.02	0.02	0.2	6	—
144	jellied	34.5	0.2	0	—	65.0	0	261	10	0.02	0.02	0.2	4	—
145	Molasses	24	2.4	0	—	60	0	240	0	0.08	0.16	2.8	0	—
Fats, Oils														
146	Butter	15.5	0.6	81	0.28	0.4	0	716	3300	trace	0.01	0.1	0	D 60 I.U. †; E 2.4
147	Cod-liver oil	0	0	100	—	0	0	902	85,000	0	0	0	0	D++++
148	Lard, cooking fats	0	0	100	—	0	0	884	0	0	0	0	0	E 50-60; F (in vegetable fats only when not hardened)
149	Margarine	15.5	0.35	85	—	0.4	0	800	3000	—	—	—	—	D
150	Mayonnaise	16	1.5	78	—	3.0	0	720	10	0.02	0.02	0.2	6	—
Milk, Dairy products, Eggs														
Butter. See under Fats														
Cheese														
151	Camembert	51	19.7	25.2	0.14	0	0	306	3610	0	0.83	1.60	0	D; E 1.0
152	Cheddar	37	25.0	32.2	—	2	0	398	1400	0.02	0.42	trace	0	—
153	Cream-	53	7.1	36.9	0.14	2	0	368	2000	0.02	0.20	0.06	0	D; E 1.0
154	Emmentaler	34	28.6	31.3	0.145	2	0	404	4010	0.03	0.45	1.24	0	D; E 1.0
155	Limburger	38	23.5	32.4	0.135	1	0	390	2000	0.02	0.2	0.06	0	D; E 1.0
156	Parmesan	29	36.3	27.4	0.19	2	0	400	1350	0.03	0.53	0.11	0	D; E 1.0
157	Roquefort	37	21.7	33.2	0.135	1	0	390	4010	0.03	0.45	1.24	0	D; E 1.0
Eggs														
158	whole, raw	74	12.8	11.5	0.463	0.7	—	158	1140	0.12	0.34	0.1	0	D+++; E 1.1
	1 egg, medium	40	6.9	6.2	0.25	0.4	—	85	615	0.06	0.18	0.05	0	D+++; E 0.6
	1 egg white, medium	27	3.3	0	0	0.3	—	15	0	0	0.07	0.02	0	—
	1 egg yolk, medium	13	3.6	6.2	0.25	0.1	—	70	615	0.06	0.11	0.03	0	—
159	dried	2	48.2	43.3	2.14	2.6	—	593	4460	0.35	1.23	0.2	0	D+++; E+++
160	Egg yolk, raw	49.4	16.3	31.9	2.0	0.7	—	355	3210	0.32	0.52	—	0	D+++; E+++
161	Egg white, raw	88	10.8	0	0	1	—	47	0	0	0.23	0.08	0	—
Milk														
(for bibliographical review see <i>J. Dairy Research.</i> , 18, 317, 1951)														
Cow's milk**														
162	fresh	87.3	3.3	3.7	0.11	4.94	0	65	130	0.04	0.16	0.09	1.8	B ₁₂ ; D; E 0.1; pant. a. 0.35
163	buttermilk	90.5	3.5	0.5	—	4.8	0	36	trace	0.04	0.18	0.1	1	0
164	condensed, sweetened ..	27.0	8.1	8.4	—	54.8	0	327	430	0.05	0.39	0.2	1	D
165	unsweetened	73.7	7.0	7.9	—	9.9	0	139	400	0.05	0.36	0.2	1	D; E 0.30

* A = vitamin-A activity due to carotenes; 1 I. U. vitamin A = 0.0006 mg β-carotene. †) In summer; in winter less.

**Content per 100 g:

	pH ¹	Spec. grav.	Casein	Albumin	Total protein	Non-protein N	Ash
Cow's milk	6.60	1.031	2.80 g	0.40 g	2.0-6.0 g	13-14 mg	0.72 g
Human milk	6.97	1.031	0.40 g	0.30 g	1.0-6.0 g	32.4 mg	0.21 g
Sheep's milk	6.54	1.036	4.17 g	0.98 g	4.5-5 g	42.5 mg	0.93 g
Goat's milk	—	1.031	2.87 g	0.89 g	3.6-3.8 g	—	0.85 g

For all other values see the table

¹) Determined on very fresh samples.

	Other organic constituents					Excess acid as N-HCl	Excess base as N-NaOH	Minerals									
	Malic acid	Citric acid	Oxalic acid	Uric acid	Purine bases			Sodium	Potassium	Calcium	Magne- sium	Manga- nese	Iron	Copper	Phospho- rus	Sulphur	Chlorine
	mg	mg	mg	mg	mg	ml	ml	Na mg	K mg	Ca mg	Mg mg	Mn mg	Fe mg	Cu mg	P mg	S mg	Cl mg
136	0	0	0	0	0	0	0	24	230	80	—	—	0	—	40	—	—
137	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
138	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
139	—	—	++	—	—	6.8	0	—	442	95	—	—	6.8	—	343	95	71
140	—	—	++	—	—	+	0	86	420	80	—	—	0.9	—	400	—	—
141	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
142	—	—	—	—	—	—	—	5	10	5	6	0.209	0.9	0.075	16	5	19
143	—	—	—	—	—	—	—	13	13	12	—	—	0.3	—	12	—	—
144	—	—	—	—	—	—	—	—	—	12	—	—	0.3	—	12	—	—
145	—	—	—	—	—	0	17.8	43	1238	273	81	—	6.7	—	51	50	501
146	0	0	0	0	0	0	0	220	14	16	1	—	0.2	—	16	9	330
147	0	0	0	0	0	0	0	0.1	0	0	0	0	0	0	0	0	0
148	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
149	0	0	0	0	0	0	0	—	—	20	—	—	0	—	16	—	—
150	0	0	0	0	0	3.5	0	600	17	19	—	—	1.0	—	60	—	—
151	0	0	0	0	0	4.5	0	340	90	680	—	—	0.9	—	500	—	—
152	0	0	0	0	0	—	—	—	—	725	—	—	1.0	—	495	—	—
153	0	0	0	0	0	4.5	0	340	90	30	—	—	0.1	—	40	—	—
154	0	0	0	0	0	6	0	420	110	1090	—	—	1.2	—	810	—	—
155	0	0	0	0	0	4.5	0	400	100	440	—	—	—	—	570	—	—
156	0	0	0	0	0	5.1	0	880	131	1220	42	—	1.9	—	770	218	1350
157	0	0	0	0	0	4.5	0	—	—	720	—	—	1.0	—	520	—	—
158	0	0	0	0	0	11.1	0	81	100	54	13	0.033	2.7	0.253	210	197	120
	0	0	0	0	0	6.0	0	44	54	29	7	0.018	1.5	0.14	114	107	65
	0	0	0	0	0	1.6	0	34	31	6	3	—	0.03	—	3	64	50
	0	0	0	0	0	4.4	0	10	23	23	4	—	1.5	—	111	43	15
159	0	0	0	0	0	+	0	—	—	187	—	—	8.7	—	800	—	—
160	0	0	0	0	0	25.6	0	26	100	147	16	—	7.2	—	586	194	124
161	0	0	0	0	0	5.2	0	110	100	20	11	—	0.1	—	10	208	161
162	—	250	0	0	0	0	4–5	58	138	125	13	0.002	0.1*	0.03	99	30	103
163	—	—	0	0	0	0	5–6	130	140	105	—	—	0.3	—	97	—	—
164	—	—	0	0	0	0	5–6	140	340	273	—	—	0.2	—	228	—	—
165	—	—	0	0	0	0	4–5	100	270	243	—	—	0.2	—	195	—	—

Normal variations in mature breast milk (after ALBRITTON, E. C., *Standard Values in Nutrition and Metabolism*, Philadelphia, 1954, and MATTICI, M. R., and BRIDGES, M. A., *Dietetics for the Clinician*, Philadelphia, 1941): proteins 1.0–6.0 g; non-protein N 0.017–0.060 g; lactose 5–9.5 g; fats 0.5–9.0 g; ash 0.1–0.5 g; chlorides (as Cl) 9–355 mg; calcium 15–61 mg; magnesium 2–6 mg; phosphorus 7–35 mg; potassium 27–81 mg; iron 0.02–0.45 mg (all per 100 ml milk). Specific gravity 1.026–1.037; pH 7–7.6.

* In commercial milk; in fresh milk less.

	Content per 100 grams edible portion (unless otherwise stated)	Water g	Proteins g	Fats		Carbo- hydrates		Calories kcal	Vitamins					
				Total g	Choles- terol g	Total g	Fibre g		A* I.U.	B ₁ mg	B ₂ mg	Nicotinic acid mg	C mg	Other vitamins (vit. E in mg)
166	Milk powder: from whole milk	3.5	25.8	26.7	—	38.0	0	496	1400	0.29	1.1–2.0	0.5–1.6	10	D
167	from skimmed milk	3.5	35.6	1.0	—	52.0	0	359	40	0.35	1.96	1.1	7	—
168	Cream, 20%	73	2.5	20.0	—	4	0	206	1250	0.03	0.13	—	1	D
169	35%	59	2.3	35.0	—	3	0	336	2250	0.03	0.15	—	1	D++
170	Cocoa made with 100% milk	—	3.3	4.3	—	12	—	100	170	0.05	0.16	0.11	0	D
171	50% milk, 50% water	—	1.8	2.5	—	10	—	68	86	0.02	0.08	0.09	0	0
172	Breast milk** (see also pages 228 and 229)	87.58	2.01	3.8	0.01	6.5	0	62	350	0.04	0.06	0.26	6	D
173	Goat's milk**	86.88	3.76	4.07	—	4.64	0	71	170	0.06	0.07	0.25	1	D+
174	Sheep's milk**	83.57	5.15	6.18	—	4.17	0	93	—	—	—	—	3.6	—
Meat, Poultry														
Beef														
175	grilled steak	57	16.9	25.0	—	0	0	293	0	0.10	0.13	4.6	0	E 0.47
176	roast, medium fat	53	15.5	31	—	0	0	341	0	0.10	0.12	4.2	0	—
177	roast, lean	67	19.3	13	—	0	0	194	0	0.12	0.15	5.2	0	—
178	raw, medium fat	60	16.9	21.0	0.125	0	0	218	20	0.20	0.29	7.0	—	—
179	stewed	70	20.3	9	—	0	0	162	0	0.13	0.16	5.5	0	—
180	corned	57.3	24.4	15	—	0	0	232	0	0.02	0.19	2.7	0	—
181	dehydrated/salted	47.7	34.3	6.3	—	0	0	194	0	0.11	9.22	3.7	0	—
182	brain	81	10.0	8.3	2.36	0	0	115	0	—	—	4.5	—	—
183	heart	75.4	16.5	6.3	0.15	0.7	0	104	0	0.54	0.89	6.8	14	—
184	kidneys	75	15.0	8.1	0.41	1	0	136	1000	0.25	2.10	7.40	11	—
185	liver	70.9	19.8	4.2	0.32	3.6	0	131	19,200	0.27	2.80	16.1	31	D; E 1.4; K
186	tongue	68	16.4	15	—	0.4	0	202	0	0.22	0.27	5.0	0	—
187	tripe	79	19.1	2.0	0.15	0	0	94	—	0.01	—	3.00	—	—
Calf														
188	brain	81	10.0	8.3	2.1	0	0	115	—	—	—	4.50	—	—
189	heart	76	15.4	7.1	0.18	1	0	130	—	0.60	—	10.60	—	—
190	kidney	76	16.9	6.4	0.5	0	0	125	1200	0.26	2.4	7.40	10	—
191	liver	71	19.0	4.9	0.36	4	0	136	27,000	0.40	3.30	12.0	32	D, E, K
192	sweetbread	75	19.6	3.1	0.28	0	0	106	—	0.06	0.27	4.10	—	—
Chicken														
193	young	75	21.6	2.7	—	0	0	111	0	0.23	0.15	6.0	—	E 0.21
194	raw	68	20.0	11.0	0.09	0	0	179	0	0.1	0.2	6.2	—	E 0.22
195	grilled	66.0	20.2	12.6	0.09	0	0	194	0	0.11	0.18	8.6	—	—
196	liver	70.0	22.1	4.0	—	3	0	136	24,000	0.40	2.50	14.60	35	D, E, K
197	Duck, medium fat, raw	54	16.0	28.6	0.07	0	0	321	—	0.13	0.41	7.89	8	—
Goose														
198	medium fat, raw	51	16.4	31.5	—	0	0	349	—	0.16	0.24	—	13	—
199	liver	67	16.5	10.0	—	5	0	176	—	0.03	—	3.6	—	D, E
200	Hare, medium fat	73	21.0	5.0	0.08	0	0	129	—	0.05	0.06	12.70	—	—
Lamb														
201	medium fat, roast	53	22.5	23.5	—	0	0	308	(0)	0.13	0.23	4.8	0	—
202	chops, grilled	40	24	35	—	0	0	418	(0)	0.14	0.26	5.6	0	—
203	Mutton, medium fat	63.7	18	17.5	0.07	0	0	230	0	0.21	0.26	5.9	0	—
Pork														
204	medium fat	58	16.4	25.0	0.9	0	0	291	0	1.04	0.20	4.4	0	B ₆ ; E 0.63
205	cutlets	53	14.6	32	0.105	0	0	346	0	0.18	0.04	0.9	0	B ₆
206	liver	72	19.6	4.8	0.42	2	0	130	2700	0.43	2.70	15.50	27	D+, E+
Ham														
207	medium fat, raw	53	15.2	31	0.105	0	0	340	0	0.96	0.19	4.1	0	E 0.44
208	smoked	42	16.9	35	—	0	0	384	0	0.78	0.19	3.8	0	E 0.44

* A = vitamin-A activity due to carotenes; 1 I. U. vitamin A = 0.0006 mg β-carotene. ** Cf. footnote ** on page 238.

	Other organic constituents					Excess acid as N-HCl	Excess base as N-NaOH	Minerals									
	Malic acid	Citric acid	Oxalic acid	Uric acid	Purine bases			Sodium	Potassium	Calcium	Magne- sium	Manga- nese	Iron	Copper	Phospho- rus	Sulphur	Chlorine
	mg	mg	mg	mg	mg	ml	ml	Na mg	K mg	Ca mg	Mg mg	Mn mg	Fe mg	Cu mg	P mg	S mg	Cl mg
166	—	—	0	0	0	0	4-5	410	1100	949	—	—	0.6	—	728	—	—
167	—	—	0	0	—	0	4-5	—	—	1300	—	—	0.6	—	1030	—	—
168	—	—	0	0	0	0	0	30	130	90	10	—	0.2	—	80	30	80
169	—	—	0	0	0	0	0	—	—	90	—	—	0.2	—	70	—	—
170	—	—	0	0	0	0	4-5	—	—	110	—	—	0.3	—	110	—	—
171	—	—	0	0	0	0	2-3	—	—	60	—	—	0.2	—	70	—	—
172	—	150	0	0	0	0	4-5	13	45	35	5	—	0.7	0.06	20	11	50
173	—	—	0	0	0	0	4-5	34	180	128	13.3	—	0.2	—	103	37	14
174	—	130	0	0	0	0	4-5	33	188	207	8.3	—	—	—	125	—	95
175	—	—	0	++	++	+	0	—	—	10	—	—	2.5	—	182	—	—
176	—	—	0	++	++	+	0	—	—	9	—	—	2.3	—	167	—	—
177	—	—	0	++	++	+	0	—	—	11	—	—	2.9	—	208	—	—
178	—	—	0	111	37	10.6	0	84	338	10	24	—	3.7	—	180	230	76
179	—	—	0	++	++	+	0	—	—	12	—	—	3.0	—	219	—	—
180	—	—	0	++	++	+	0	1700	400	29	—	—	4.0	—	113	—	—
181	—	—	0	+++	+++	+	0	3900	1000	20	—	—	5.1	—	370	—	—
182	—	—	0	84	28	+	0	90	340	11	—	—	1.6	—	360	—	—
183	—	—	0	++	++	9.1	0	70	380	10	40	—	6.2	—	236	296	122
184	—	—	0	240	80	7.6	0	246	238	10	21	—	6.5	—	260	190	246
185	—	—	0	279	93	8.5	0	87	298	8	22	0.3	12.1	3.5	373	251	101
186	—	—	0	++	++	7.8	0	100	260	30	—	—	6.9	—	119	—	—
187	—	—	0	++	++	+	0	46	19	10	—	—	1.6	—	130	—	—
188	—	—	0	75	26	+	0	110	305	11	—	—	1.5	—	360	—	—
189	—	—	0	++	++	8.5	0	71	370	11	35	—	6.2	—	240	296	125
190	—	—	0	+++	+++	+	0	—	—	9	—	—	4.1	—	171	—	—
191	—	—	0	260	88	8.2	0	87	298	11	22	0.341	5.4	3.451	210	251	101
192	—	—	0	990	330	+	0	—	—	11	—	—	1.6	—	—	—	—
193	—	—	0	174	58	+	0	—	—	10	—	—	3.0	—	230	—	—
194	—	—	0	87	29	10.7	0	75	372	10	27	—	3.0	—	220	252	79
195	—	—	0	++	++	+	0	—	—	16	—	—	1.9	—	218	—	—
196	—	—	0	279	93	+	0	—	—	20	—	—	—	—	240	—	—
197	—	—	0	++	++	+	0	82	285	10	—	—	1.7	—	197	—	—
198	—	—	0	99	33	7.7	0	—	—	10	—	—	2.0	—	180	—	—
199	—	—	0	260	85	+	0	—	—	10	—	—	—	—	180	—	—
200	—	—	0	++	38	14.8	0	—	—	10	—	—	3.2	—	239	—	—
201	—	—	—	—	—	—	—	—	—	9.5	—	—	2.8	—	222	—	—
202	—	—	—	—	—	—	—	—	—	11	—	—	3.0	—	200	—	—
203	—	—	0	++	++	9.3	0	84	301	10	24	—	2.7	—	194	211	85
204	—	—	0	123	41	10.0	0	69	304	10	24	—	2.5	—	177	206	69
205	—	—	0	++	++	+	0	42	169	8	12	—	2.2	—	157	115	38
206	—	—	0	+++	+++	+	0	—	—	10	—	—	—	—	210	—	—
207	—	—	0	++	++	11.9	0	—	350	9	15	—	2.3	—	164	200	—
208	—	—	0	72	24	12.5	0	2100	610	10	20	—	2.5	—	182	225	—

Content per 100 grams edible portion (unless otherwise stated)		Water	Proteins	Fats		Carbo- hydrates		Calories	Vitamins						
				Total	Choles- terol	Total	Fibre		A*	B ₁	B ₂	Nicotinic acid	C	Other vitamins	
															g
g	g	g	g	g	g	g	g	kcal							
Bacon															
209	medium fat, raw	20	9.1	65	—	1.1	0	630	(0)	0.38	0.12	1.9	0	—	
210	grilled	13	25	55	—	1.0	0	607	(0)	0.48	0.31	4.8	0	—	
211	Rabbit, medium fat	68	20.8	10.2	0.05	0	0	175	—	0.05	0.06	12.70	4	—	
Sausages															
212	beef (meat only)	55	16	28	—	0	0	316	0	0.10	0.13	4.3	0	—	
213	pork (meat only)	41.9	10.8	44.8	—	0	0	446	0	0.22	0.15	2.3	0	—	
214	Frankfurter, Vienna	64.3	15.2	14.1	—	0	0	201	0	0.19	0.23	2.4	0	—	
215	liver	59	16.7	20.6	—	2	0	260	10,000	0.19	1.30	5.20	—	D, E	
216	salami	31	23.9	36.8	—	0	0	427	—	0.24	0.21	2.91	—	—	
Sheep's offal															
Values as for Calf's offal															
217	Turkey, medium fat, raw ..	58.3	20.1	20.2	—	0	0	262	trace	0.12	0.19	7.9	—	—	
Veal															
218	lean, roasted	—	32.2	11.3	—	0	0	231	—	0.24	0.26	7.60	—	—	
219	medium fat, raw	69	19.2	11	0.065	0	0	176	0	0.18	0.27	6.3	0	—	
220	cutlets, raw	70	19.5	9	0.10	0	0	159	0	0.18	0.28	6.4	0	—	
221	Venison	73	20.0	6.0	—	0	0	134	—	—	—	—	—	—	
Fish, Sea foods															
222	Caviar, pressed	36	34.4	16.7	—	0	0	288	—	—	—	—	—	D ⁺⁺ , E ⁺⁺	
223	Cod, fresh	82.6	16.5	0.4	0.05	0	0	70	0	0.10	0.07	2.17	2	D	
224	Eel, smoked	50	18.6	27.8	—	0	0	325	2500	0.14	0.07	—	—	D	
225	Flounders	83	14.9	0.5	—	0	0	64	—	0.08	0.20	3.84	—	D	
226	Haddock, fresh	77	16.8	0.3	—	0	0	74	0	0.09	0.12	0.90	0	E 0.35	
227	Halibut	75.5	18.6	5.2	—	0	0	121	10	0.09	0.17	3.00	—	—	
228	Herrings, fresh	73	19.0	6.7	—	0	0	136	68	0.01	0.28	3.50	—	D, E	
Lobster															
229	fresh	79	16.2	1.9	0.145	1	0	86	—	0.15	0.18	—	—	—	
230	tinned	77	18.4	1.3	0.12	0.4	0	86	—	0.15	0.18	—	—	—	
231	Oysters	87.1	6.0	1.2	0.23	3.7	0	50	—	0.18	0.23	1.2	—	—	
Salmon															
232	fresh	66	22.0	12.3	0.06	0	0	203	285	0.21	0.20	7.10	9	D ⁺ , E	
233	tinned	67.4	20.6	9.6	—	0	0	169	80	0.03	0.18	6.5	0	D ⁺ , E	
Sardines, tinned:															
234	whole contents	47.1	21.1	27	—	1	0	331	710	0.05	0.10	4.3	0	D	
235	less excess oil	57.4	25.7	11.0	—	1.2	0	207	290	0.06	0.12	5.2	0	D	
236	Shrimps, tinned	78.8	17.8	0.8	0.15	0.8	—	82	60	0.01	0.03	1.9	0	—	
237	Trout	78	19.2	2.1	—	0	0	96	12	0.09	0.05	3.50	—	—	
238	Tunny, tinned	57.7	27.7	11.8	—	0	0	217	70	0.04	0.13	10.6	0	D	
Miscellaneous															
239	Cocoa powder	4.3	9.0	18.8	—	31.0	—	329	0	0.09	0.45	1.50	0	E 3.1	
240	Gelatin, dry	13	85.6	0.1	—	0	0	343	0	0	0	0	0	0	
241	Mushrooms	90.0	3.5	0.4	—	6.0	0.8	42	0	0.11	0.42	6.37	5	—	
Yeast															
242	dried	7.0	46.1	1.6	0.68	0	0	348	0	9.69	5.45	36.2	0	} whole B complex	
243	pressed	70.9	13.3	0.4	—	0	0	109	0	0.45	2.07	28.2	0		
Beverages															
244	Beer	—	0.6	4.4	0	4.0	0	50	—	0	0.03	0.79	—	—	
245	Brandy	—	—	40	0	—	0	250	0	0	0	0	0	0	
246	Lemonade, average	—	0	0	0	12	0	48	0	0	0	0	0	—	
247	Port wine	—	0.3	15.0	0	14.0	0	163	—	—	—	—	—	—	
248	Rum	—	0	43.9	0	0	0	312	0	0	0	0	0	0	
249	Whisky	0	0	42.2	0	0	0	301	0	0	0	0	0	0	
250	Wine, average	—	—	7.5	0	0.1	0	53	{ red 0 white	3.5 µg	27 µg	0.16	0	—	
										0.8 µg	11 µg	0.07	0	—	

Bibliography: * A = vitamin-A activity due to carotenes; 1 I. U. vitamin A = 0.0006 mg β-carotene.

ALBRITTON, E. C., *Standard Values in Nutrition and Metabolism*, Philadelphia, 1954. BOOHER, L. E., HARTZLER, E. R., and HEWSTON, E. M., *A Compilation of the Vitamin Values of Foods in Relation to Processing and other Variants*, U. S. Department of Agriculture, Circular No. 638, Washington, 1942. BOWES, A. de P., and CHURCH, C. F., *Food Values of Portions Commonly Used*, Philadelphia, 1944. BRIDGES, M. A., and MATTICE, M. R., *Food and Beverage Analysis*, Philadelphia, 1942. CATFIELD, C., *Food Composition Tables for International Use*, Food and Agriculture Organization of the United Nations, Rome, 1949. CAILLAUX and RELDA, *Bull. Acad. Méd.*, **133**, 204, 1949. CATFIELD, C., and ADAMS, G., *Proximate Composition of American Food Materials*, U. S. Department of Agriculture, Circular No. 549, Washington, 1940. CLOUSE, R. C., *Compilation of Recent Data on Mineral and Vitamin Values of Foods*, *J. Amer. diet. Ass.*, **19**, 496-504, 746-755, 1943. DEMOLE, J., FLEISCH, A., and PETITPIERRE, C., *Ernährungslehre und Diätetik*, Berne, 1948. ELVEHIEM and PAVCEK, *Table of Proximate Mineral and Vitamin Composition of Foods*, Committee of the Food and Nutrition Board, National Research

	Other organic constituents					Excess acid as N-HCl	Excess base as N-NaOH	Minerals									
	Malic acid	Citric acid	Oxalic acid	Uric acid	Purine bases			Sodium	Potassium	Calcium	Magne- sium	Manga- nese	Iron	Copper	Phospho- rus	Sulphur	Chlorine
	mg	mg	mg	mg	mg	ml	ml	Na mg	K mg	Ca mg	Mg mg	Mn mg	Fe mg	Cu mg	P mg	S mg	Cl mg
209	—	—	—	—	—	—	—	—	—	13	—	—	0.8	—	108	—	—
210	—	—	—	—	—	—	—	—	—	25	—	—	3.3	—	255	—	—
211	—	—	0	++	++	14.8	0	40	390	10	—	—	3.1	—	220	—	—
212	—	—	—	++	++	+	0	—	—	9	—	—	2.4	—	172	—	—
213	—	—	—	++	++	+	0	—	—	6	—	—	1.6	—	116	—	—
214	—	—	—	++	++	+	0	—	—	9	—	—	2.3	—	164	—	—
215	—	—	—	114	38	+	0	—	—	10	—	—	2.5	—	180	—	—
216	—	—	—	++	23	+	0	—	—	10	—	—	3.6	—	260	—	—
217	—	—	0	++	++	+	0	66	367	23	28	—	3.8	—	320	234	123
218	—	—	0	++	++	+	0	—	—	20	—	—	3.6	—	290	—	—
219	—	—	0	114	38	9.8	0	48	359	11	23	—	2.9	—	207	203	77
220	—	—	0	++	++	+	0	—	—	11	—	—	2.9	—	210	—	—
221	—	—	0	117	39	+	0	—	—	11	—	—	3.0	—	220	—	—
222	—	—	—	0	0	+	0	2200	640	140	—	—	—	—	180	—	—
223	—	—	—	114	38	5.5	0	96	339	18	22	—	0.9	—	189	203	150
224	—	—	—	81	27	9.9	0	—	—	0.02	—	—	1.0	—	210	—	—
225	—	—	—	++	++	7.1	0	107	311	30	25	—	1.0	—	160	217	151
226	—	—	—	117	39	16.1	0	660	314	19	26	0.015	0.9	0.216	190	238	1070
227	—	—	—	++	++	9.4	0	83	340	20	24	0.010	0.9	0.160	213	212	88
228	—	—	—	207	69	+	0	—	—	20	—	—	1.1	—	220	—	—
229	—	—	—	66	22	8.5	0	210	180	60	—	—	0.8	—	280	—	—
230	—	—	—	++	++	+	0	—	—	60	—	—	0.8	—	280	—	—
231	—	—	—	87	29	15.2	0	471	204	68	39	0.295	7.1	3.623	172	180	628
232	—	—	—	72	24	11.0	0	48	316	24	29	—	0.8	—	253	226	—
233	—	—	—	++	++	+	0	470	330	67	30	—	1.3	—	286	260	—
234	—	—	—	354	118	12.5	0	760	260	29	—	—	1.5	—	299	—	—
235	—	—	—	++++	++++	+	0	820	310	35	—	—	1.8	—	365	—	—
236	—	—	—	60	20	8.5	0	—	404	75	74	—	2.0	—	210	—	—
237	—	—	—	168	56	8.9	0	80	334	20	26	—	1.1	—	220	224	105
238	—	—	—	++	++	+	0	540	480	34	—	—	1.7	—	290	—	—
239	—	—	++++	—	—	—	—	55	900	160	420	—	2.7	—	709	203	51
240	0	0	0	—	—	—	—	27	—	11	—	—	0	—	0	—	—
241	—	—	—	54	18	4.0	0	5	520	10	16	—	0.7	—	100	51	21
242	—	—	—	—	—	—	—	180	1900	106	—	—	18.2	—	1893	—	—
243	—	—	—	—	—	—	—	—	—	25	—	—	4.9	—	605	—	—
244	—	—	—	—	—	—	—	8	46	10	—	—	0	—	20	—	—
245	0	0	0	0	0	0	0	—	—	—	—	—	—	—	—	—	—
246	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
247	+	+	+	0	0	0	0	—	—	—	—	—	—	—	—	—	—
248	0	0	0	0	0	0	0	—	—	—	—	—	—	—	—	—	—
249	0	0	0	0	0	0	0	—	—	—	—	—	—	—	—	—	—
250	+	+	+	0	0	0	0	7	104	10	7	—	0	—	10	15	2

Council, USA, 1948. *Handbook of Chemistry and Physics*, Cleveland, 1954–55. LANGE, N. A., and FORKER, M. G., *Handbook of Chemistry*, Sandusky, 1949. *Mayo Clinic Diet Manual*, Philadelphia, 1954. MUNSELL, H. E., The Vitamin A, Vitamin B, Vitamin C and Riboflavin Content of Common Foods, *Milbank mem. Fd. Quart.*, **21**, 102–108, 1943. NESENI and KÖPRICH, *Milchwissenschaft*, **3**, 186, 1948. OKEY, R., *J. Amer. diet. Ass.*, **21**, 342, 1945. PROUDFIT, F. T., and ROBINSON, C. H., *Nutrition and Diet Therapy*, New York, 1946. SHERMAN, H. C., and GETTLER, A. O., The Balance of Acid-Forming and Base-Forming Elements in Foods, and its Relation to Ammonia Metabolism, *J. biol. Chem.*, **11**, 323, 1912. SHERMAN, H. C., *Chemistry of Food and Nutrition*, New York, 1946. STERN, F., *Applied Dietetics*, Baltimore, 1943. TURNER, D., *Handbook of Diet Therapy*, Chicago, 1946. WALLER, D. S., *Nutrition Value of Foods*, 1939, 1949, 1950, 1951, 1952. *J. Nutr.*, *Z. Vitaminforsch.*, *J. Amer. diet. Ass.* and *J. Dairy Research*. WATT, B. K., and MERRILL, A. L., *Composition of Foods*, U. S. Department of Agriculture, Agriculture Handbook No. 8, Washington, 1950.

Definition: The basal metabolism (or basic metabolic rate, B.M.R.) is the minimal heat produced by the fasting individual, physically and mentally at rest, at room temperature (ca. 20°C). It represents the energy expended to maintain the vegetative functions, such as respiration, circulation, body temperature, etc.

The basal metabolism is primarily dependent on the surface area of the body, therefore on age and sex (see the ideal values of various standards on the following pages). It is physiologically increased during menstruation and pregnancy (see the adjacent diagram and page 248).

Variations up to $\pm 10\%$ of the ideal value are regarded as normal, occasionally also larger variations (the probability of the normality of an observed B.M.R. value can be read off directly from the nomogram on page 249).

The basal metabolism is usually pathologically increased in hyperthyreosis and fever and often in leukaemia; it is depressed in hypothyreosis and certain forms of asthenia.

The determination of basal metabolism is widely regarded as the principal aid in the differential diagnosis of hyperthyroidism. It is unreliable for this purpose, however, since there are numerous exceptions to the rule, both in the positive and negative sense, e.g. increase of basal metabolism in hyperactivity of the adrenal cortex, in which even hypoactivity of the thyroid can occur. In practice it is almost impossible to establish the conditions necessary for an accurate determination of basal metabolism (complete physical and mental relaxation), especially with children. The diagnosis of hypo- and hyper-thyroidism is therefore coming more and more to depend on other methods, such as determination of the protein-bound iodine (see page 329) or, preferably, the reaction of the thyroid to the accumulation of radioactive iodine (see page 208). It must be emphasized that the basal metabolism is no criterion in the diagnosis of hyperthyreosis and is only of value as a part of the overall clinical picture.

Determination of basal metabolism

The calorimetric determination of basal metabolism requires complicated apparatus. In practice therefore it is usually calculated from the oxygen consumption, the CO₂-liberation, and in certain cases where great accuracy is required, from the amount of urea eliminated in the urine.

The ratio of the CO₂ liberated to the oxygen consumed is known as the **respiratory quotient (RQ)**:

$$\text{CO}_2 \text{ (vol.)} / \text{O}_2 \text{ (vol.)} = \text{RQ}$$

The RQ is a measure of the metabolism of the organism.

- 1. **Approximate determination of basal metabolism** by measuring the oxygen consumption alone (on the assumption of a mean RQ of 0.82 and neglecting the nitrogen metabolism): 1 litre of O₂ consumed = a basal metabolism of 4.825 kilocalories; for conversion into oxygen consumption per square metre per minute and use of the nomogram, see page 249. This method is simple and rapid but not very reliable.
- 2. **A more exact method** is by measurement of the oxygen consumption and the RQ, with neglect of the nitrogen metabolism: from the observed value for the RQ, table 2 (opposite) then gives the number of calories per litre of oxygen consumed, and thence the calories per hour. This method is usually of sufficient accuracy (with a normal diet) for clinical purposes.
- 3. **Accurate determination** of the basal metabolism, taking into account the nitrogen metabolism:
 - a) The urea excretion is measured on the basis of the 24-hour urine volume. 1 gram of urea excreted per hour corresponds to the production of 26.54 kilocalories per hour (after LOEWY) and to an oxygen consumption of 5.939 litres per hour (in the nitrogen metabolism). These two values are designated **cal/hour (N)** and **O₂/hour (N)**.
 - b) The RQ and the oxygen consumption are now measured in the normal way and the latter value converted into litres per hour, designated **O₂/hour (total)**. Subtracting:
$$\text{O}_2/\text{hour (total)} \text{ minus } \text{O}_2/\text{hour (N)} = \text{O}_2/\text{hour (c/hydrates + fats)}.$$
 - c) The calorie value corresponding to the O₂/hour (c/h + fats) is obtained from table 2 (opposite) from the observed RQ value = **cal/hour (c/h + fats)**.

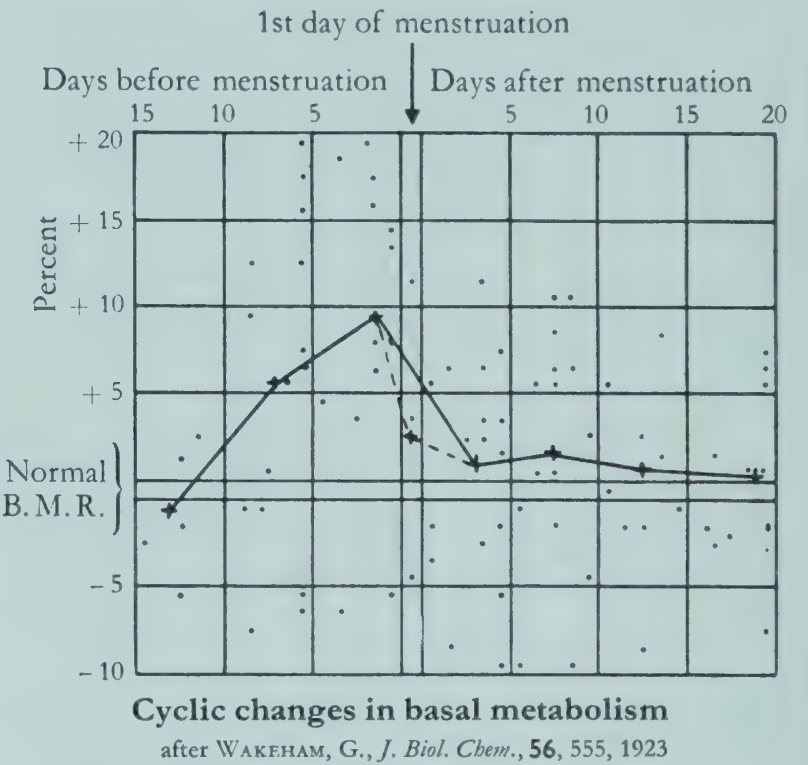
The basal metabolism is given by **cal/hour (c/h + fats) + cal/hour (N) = cal/hour (total)**.

*These methods are not valid for diabetics
(exact determination only possible by means of calorimetry)
The measured oxygen volumes must always be reduced to normal
(see page 127) before being converted into calories.*

4. Comparison of the observed basal metabolism with normal standards (ideal values).

Various standards are in use, the commonest (for adults) being those of HARRIS and BENEDICT, AUB and DUBOIS, and BOOTHBY et al. There are special standards for children (see the following pages). It is now recognized that the older standards are at too high a level owing to their having been based on tests on untrained subjects.

- a) **HARRIS-BENEDICT Standard** (page 246). This is based on biometric measurements. Bases of comparison: total calories per hour, height, weight and age of the subject.



b) *Standards giving the calorie values per square metre body surface per hour* (BOOTHBY et al., AUB and DUBOIS, etc., see the following pages). Cf. nomogram of BOOTHBY et al., page 249.

Bases of comparison: calories per square metre per hour, age and sex of the subject.

For calculation of body surface from height and weight, see nomogram on page 250.

Table 1. Calorie values, oxygen consumption and carbon dioxide liberation per gram of proteins, fats and carbohydrates consumed in the body, and per gram of urea excreted in urine¹.

1 gram	Oxygen consumed ccm	Carbon dixide liberated ccm	RQ	Calories (kcal)		Oxygen litres	Carbon dioxide litres
				after RUBNER	after LOEWY		
Proteins	966.3	773.9	0.801	4.10	4.316	4.485	5.579
Urea	5939.0	4757.0	0.801	25.63	26.54	4.485	5.579
Fats	2019.3	1427.3	0.707	9.3	9.461	4.686	6.629
Carbohydrates	828.8	828.8	1.000	4.1	4.182	5.047	5.047

Table 2. RQ, calories per litre oxygen consumed and percentage participation of carbohydrates and fats in oxygen consumption and in calorie production².

Respiratory quotient	Percentage participation in total oxygen consumption		Percentage participation in total calorie production		Calories per litre oxygen	
	Carbohydrates	Fats	Carbohydrates	Fats	kcal	log ₁₀ *
	(1)	(2)	(3)	(4)	(5)	
0.707	0	100.0	0	100.0	4.686	0.6708
0.71	1.02	99.0	1.10	98.9	4.690	0.6711
0.72	4.44	95.6	4.76	95.2	4.702	0.6723
0.73	7.85	92.2	8.40	91.6	4.714	0.6734
0.74	11.3	88.7	12.0	88.0	4.727	0.6746
0.75	14.7	85.3	15.6	84.4	4.739	0.6757
0.76	18.1	81.9	19.2	80.8	4.751	0.6768
0.77	21.5	78.5	22.8	77.2	4.764	0.6779
0.78	24.9	75.1	26.3	73.7	4.776	0.6791
0.79	28.3	71.7	29.9	70.1	4.788	0.6802
0.80	31.7	68.3	33.4	66.6	4.801	0.6813
0.81	35.2	64.8	36.9	63.1	4.813	0.6824
0.82	38.6	61.4	40.3	59.7	4.825	0.6835
0.83	42.0	58.0	43.8	56.2	4.838	0.6846
0.84	45.4	54.6	47.2	52.8	4.850	0.6857
0.85	48.8	51.2	50.7	49.3	4.862	0.6868
0.86	52.2	47.8	54.1	45.9	4.875	0.6879
0.87	55.6	44.4	57.5	42.5	4.887	0.6890
0.88	59.0	41.0	60.8	39.2	4.899	0.6901
0.89	62.5	37.5	64.2	35.8	4.911	0.6912
0.90	65.9	34.1	67.5	32.5	4.924	0.6923
0.91	69.3	30.7	70.8	29.2	4.936	0.6934
0.92	72.7	27.3	74.1	25.9	4.948	0.6945
0.93	76.1	23.9	77.4	22.6	4.961	0.6955
0.94	79.5	20.5	80.7	19.3	4.973	0.6966
0.95	82.9	17.1	84.0	16.0	4.985	0.6977
0.96	86.3	13.7	87.2	12.8	4.998	0.6988
0.97	89.8	10.2	90.4	9.58	5.010	0.6998
0.98	93.2	6.83	93.6	6.37	5.022	0.7009
0.99	96.6	3.41	96.8	3.18	5.035	0.7020
1.00	100.0	0	100.0	0	5.047	0.7030

Equations for table 2:

Column 1: percentage = 100 $\frac{RQ - 0.707}{0.293}$

Column 2: percentage = 100 $\frac{1 - RQ}{0.293}$

Column 3: percentage = $\frac{504.7 (RQ - 0.707)}{5.047 (RQ - 0.707) + 4.686 (1 - RQ)}$

Column 4: percentage = $\frac{468.6 (1 - RQ)}{5.047 (RQ - 0.707) + 4.686 (1 - RQ)}$

Column 5: calories (kcal) = $4.686 + \frac{RQ - 0.707}{0.293} \times 0.361$

* For logarithms see pages 8-15.

¹) After PETERS and VAN SLYKE, *Quantitative Clinical Chemistry*, Baltimore, 1946.

²) After ZUNTZ and SCHUMBURG, modified by LUSK, G., *J. biol. Chem.*, **59**, 41, 1924.

Harris-Benedict Standard for normal (total) calorie consumption per hour

(after ROTH, P., *Metabolimetric Compendium*, New York, 1924)

The table is based on the following equation: Men: $C = 66.473 + 13.751 W + 5.0033 H - 6.7550 A$
Women: $C = 655.0955 + 9.5634 W + 1.8496 H - 4.6756 A$
(C = total kilocalories in 24 hours, W = weight in kilograms, H = height in centimetres, A = age in years.)

The normal calorie consumption per hour is obtained by adding the values in table 1 to the corresponding values in table 2. In table 1 the values corresponding to the odd weight figures are obtained by interpolation.

Table 1. Calories according to weight

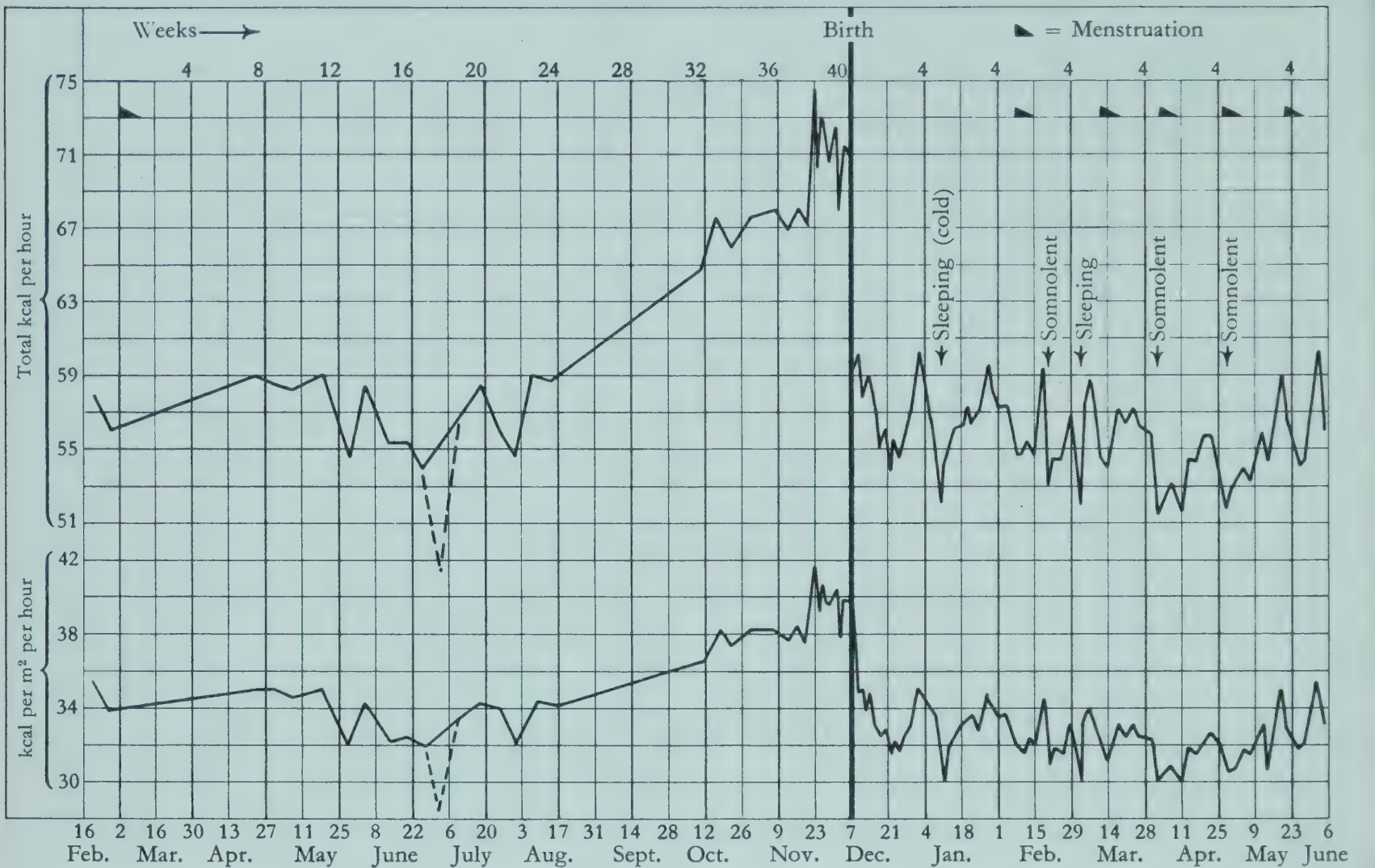
Weight			Total kcal per hour		Weight			Total kcal per hour	
lb.	kg		Males	Females	lb.	kg		Males	Females
22	10	8.5	—	159	72	44.0	56.0
26	12	9.7	—	163	74	45.2	56.8
31	14	10.8	—	167	76	46.3	57.6
35	16	12.0	—	172	78	47.5	58.4
40	18	13.1	—	176	80	48.6	59.2
44	20	14.3	—	181	82	49.7	60.0
48	22	15.4	—	185	84	50.9	60.8
53	24	16.6	—	190	86	52.0	61.6
57	26	17.7	37.6	194	88	53.2	62.4
62	28	18.8	38.4	198	90	54.3	63.2
66	30	19.9	39.2	203	92	55.5	64.0
70	32	21.1	40.0	207	94	56.6	64.8
75	34	22.2	40.8	212	96	57.8	65.6
79	36	23.4	41.6	216	98	58.9	66.4
84	38	24.5	42.4	220	100	60.1	67.2
88	40	25.7	43.2	225	102	61.2	68.0
93	42	26.8	44.0	229	104	62.4	68.8
97	44	28.0	44.8	234	106	63.5	69.6
101	46	29.1	45.6	238	108	64.7	70.4
106	48	30.3	46.4	242	110	65.8	71.2
110	50	31.4	47.2	247	112	67.0	72.0
115	52	32.6	48.0	251	114	68.1	72.8
119	54	33.7	48.8	256	116	69.3	73.6
123	56	34.9	49.6	260	118	70.4	74.4
128	58	36.0	50.4	264	120	71.6	75.2
132	60	37.2	51.2	269	122	72.7	76.0
137	62	38.3	52.0	273	124	73.9	76.8
141	64	39.5	52.8	278	126	75.0	77.6
146	66	40.6	53.6	282	128	76.1	78.4
150	68	41.8	54.4	286	130	77.2	79.2
154	70	42.9	55.2					

Table 2. Calories (kcal) according to age and height
Men

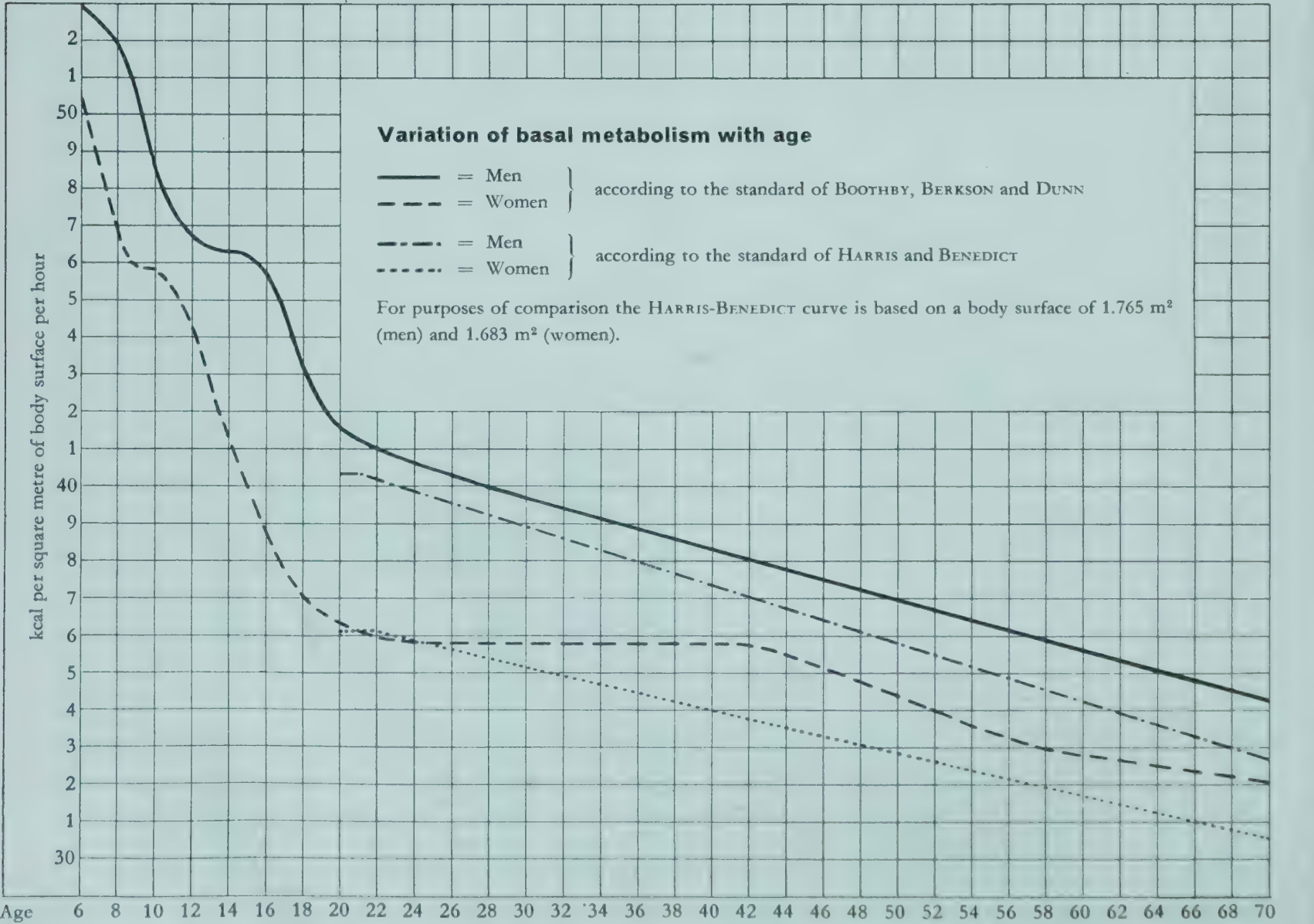
in.	cm	Age 20	Age 25	Age 30	Age 35	Age 40	Age 45	Age 50	Age 55	Age 60	Age 65	Age 70
59	150	. .	25.6	24.2	22.8	21.4	20.0	18.6	17.2	15.8	14.4	13.0
61	155	. .	26.6	25.2	23.8	22.4	21.0	19.6	18.2	16.8	15.4	14.0
63	160	. .	27.7	26.3	24.9	23.5	22.1	20.7	19.3	17.9	16.5	15.1
65	165	. .	28.7	27.3	25.9	24.5	23.1	21.7	20.3	18.9	17.5	16.1
67	170	. .	29.8	28.4	27.0	25.6	24.2	22.8	21.4	20.0	18.6	17.2
69	175	. .	30.8	29.4	28.0	26.6	25.2	23.8	22.4	21.0	19.6	18.2
71	180	. .	31.9	30.4	29.1	27.6	26.2	24.8	23.4	22.0	20.6	19.2
73	185	. .	32.9	31.5	30.1	28.7	27.3	25.9	24.5	23.1	21.7	20.3
75	190	. .	34.0	32.5	31.2	29.7	28.3	26.9	25.5	24.1	22.7	21.3
77	195	. .	35.0	33.6	32.2	30.8	29.4	28.0	26.6	25.2	23.8	22.4
79	200	. .	36.1	34.6	33.2	31.8	30.4	29.0	27.6	26.2	24.8	23.4

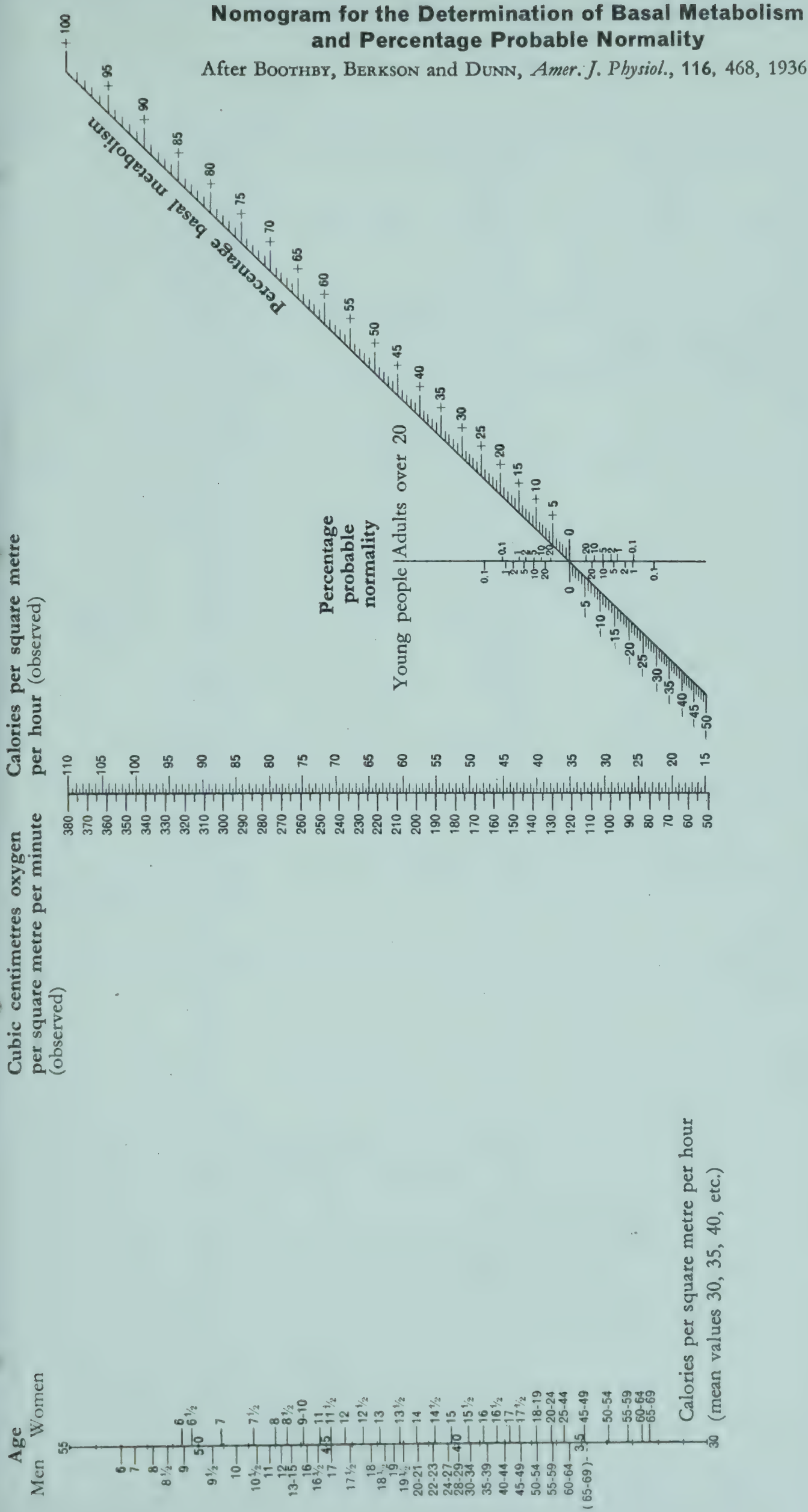
Women

59	150	. .	7.7	6.7	5.7	4.7	3.8	2.8	1.8	0.9	0.0	-1.0	-2.0
61	155	. .	8.1	7.1	6.1	5.1	4.2	3.2	2.2	1.2	0.2	-0.7	-1.7
63	160	. .	8.5	7.5	6.5	5.5	4.5	3.6	2.6	1.6	0.6	-0.3	-1.3
65	165	. .	8.8	7.8	6.9	5.9	4.9	4.0	3.0	2.0	1.0	0.0	-0.9
67	170	. .	9.2	8.2	7.3	6.3	5.3	4.3	3.4	2.4	1.4	0.5	-0.5
69	175	. .	9.6	8.6	7.6	6.7	5.7	4.7	3.7	2.8	1.8	0.8	-0.2
71	180	. .	10.0	9.0	8.0	7.0	6.1	5.1	4.1	3.2	2.2	1.2	0.2
73	185	. .	10.4	9.4	8.4	7.5	6.5	5.5	4.5	3.5	2.6	1.6	0.6
75	190	. .	10.8	9.8	8.8	7.8	6.8	5.9	4.9	3.9	3.0	2.0	1.0
77	195	. .	11.2	10.2	9.2	8.2	7.2	6.2	5.3	4.3	3.3	2.4	1.4
79	200	. .	11.5	10.5	9.6	8.6	7.6	6.7	5.7	4.7	3.7	2.7	1.8



Basal metabolism before, during and after pregnancy: the upper curve gives the total calories, the lower curve the calories per square metre of body surface calculated from the DUBOIS formula. After SANDIFORD, I., and WHEELER, T., *J. biol. Chem.*, 62, 329, 1924.

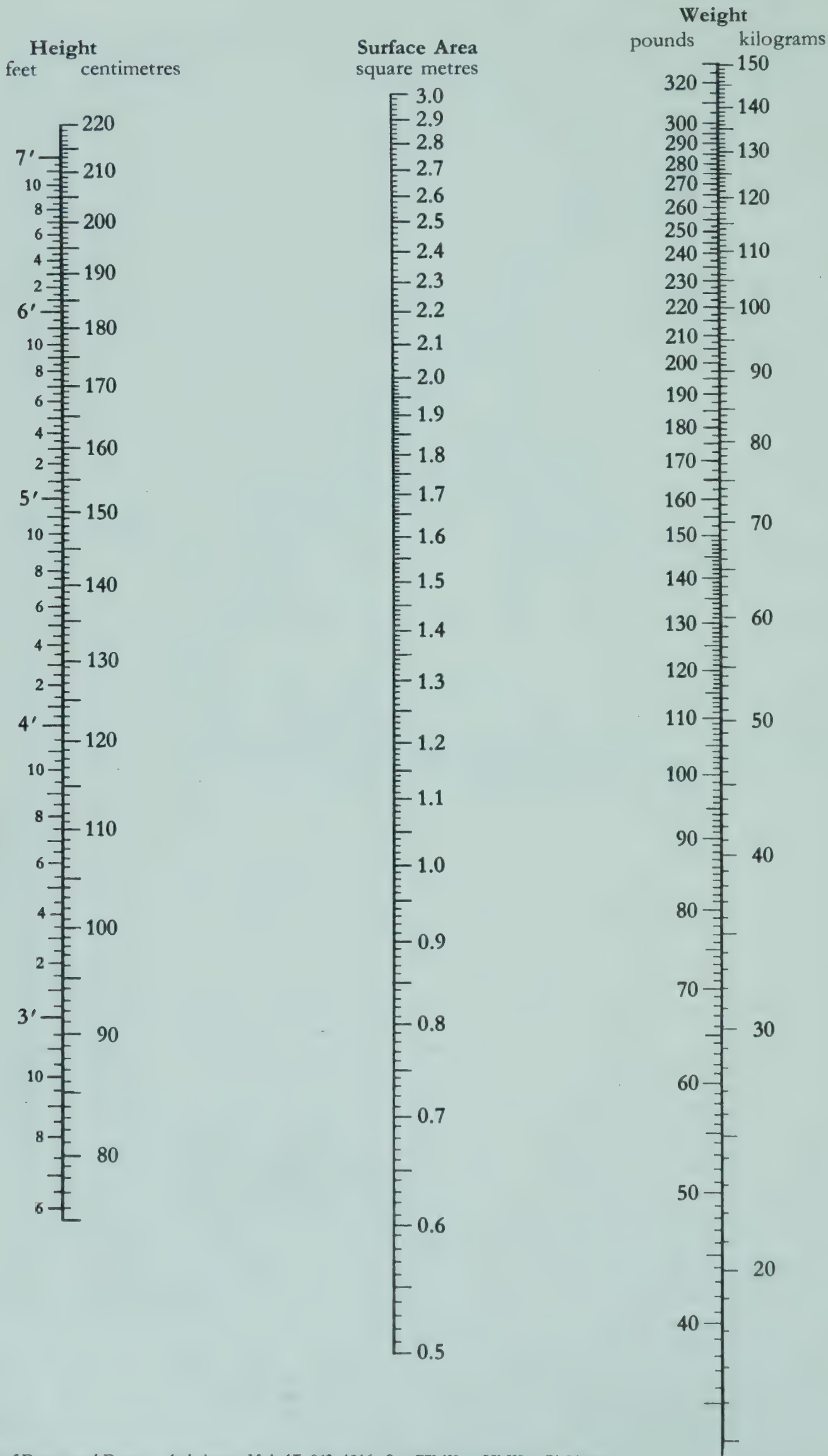




Use of the nomogram:

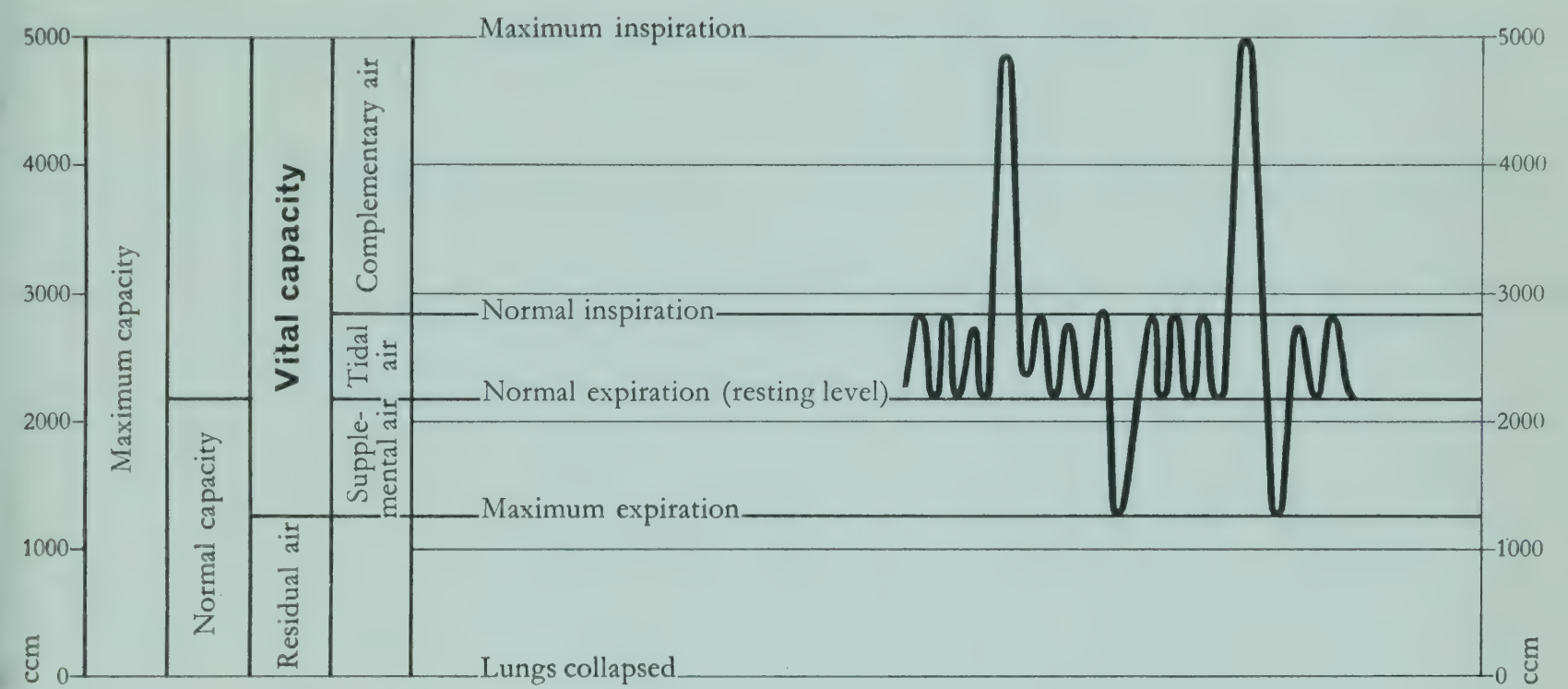
1. *Determination of the percentage basal metabolism on the assumption of an average RQ:* draw a straight line between the appropriate point on the age scale and the observed oxygen consumption per square metre per minute. The point at which this line intersects the right-hand oblique scale gives the percentage basal metabolism.
2. *Determination of the basal metabolism from the calories per square metre per hour* (i.e. taking the RQ into account, and either neglecting or allowing for the nitrogen metabolism): draw a line through the appropriate points and read off as in 1.
3. *Probable normality:* this is given by the intersection of the above-mentioned straight lines with the small vertical scale on the right. A probable normality of 0.1%, for example, means that in the examination of 1000 normal persons the observed basal metabolism value is to be expected in the case of one person.

Nomogram for Determination of Body Surface Area
from Height and Weight¹



¹) From the formula of DUBOIS and DUBOIS, *Arch. intern. Med.*, **17**, 863, 1916: $S = W^{0.425} \times H^{0.725} \times 71.84$, or:
 $\log S = 0.425 \log W + 0.725 \log H + 1.8564$.
(S = body surface in square centimetres, W = weight in kilograms, H = height in centimetres.)

Definition :

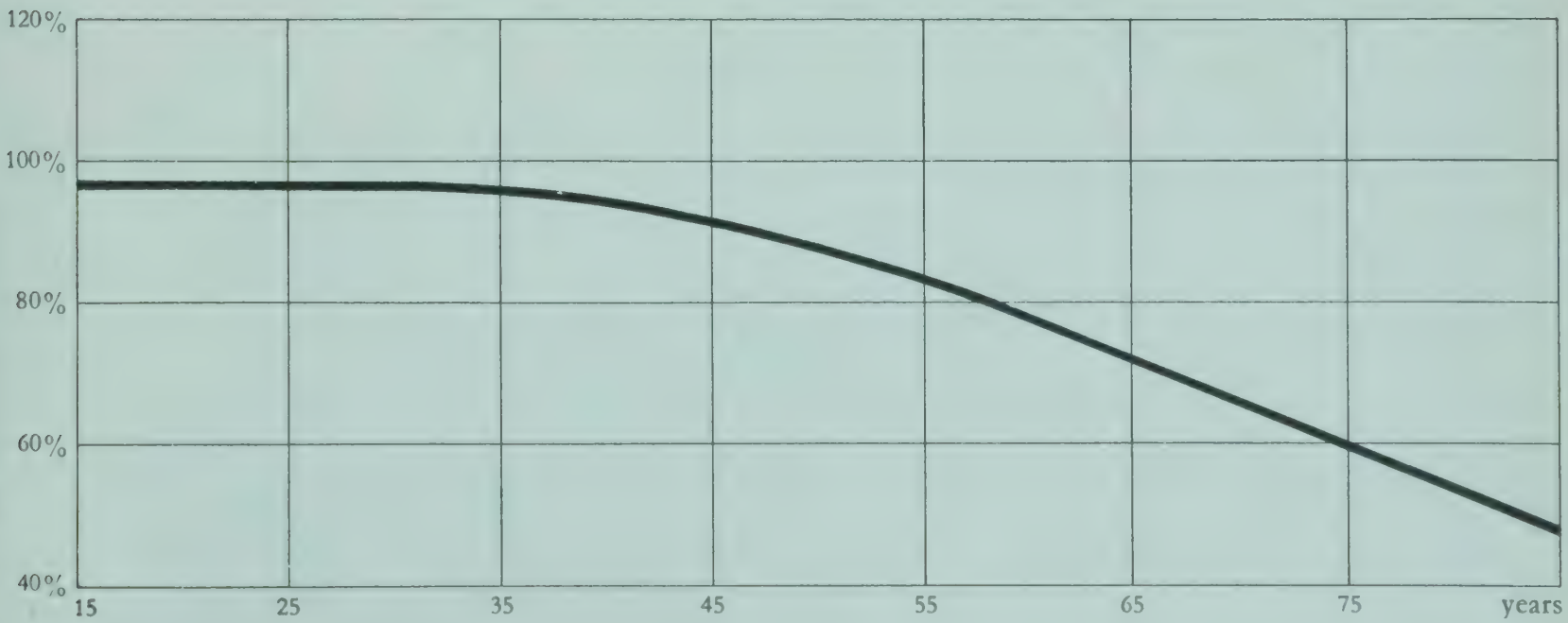


According to HENDERSON and HAGGARD, *Noxious Gases*, New York, 1943, the normal respiratory volume amounts to :

Fasting, resting in bed	6 litres per minute at 20° C
Sitting	7 " " " "
Standing	8 " " " "
Walking at about 2 m.p.h.	14 " " " "
Walking at about 4 m.p.h.	26 " " " "
Running	43 " " " "
In extreme physical exertion	65-100 " " " "

For increase of vital capacity in youth, see page 254; the respiratory volume falls gradually with advancing age (see diagram below).

Measured values for vital capacity are best compared with the ideal values on the basis of body surface area (calculated from weight and height using the DUBOIS formula and the nomogram opposite).



Diminution of vital capacity with age
After BOWEN and DUBOIS, *Arch. intern. Med.*, 17, 863, 1916

252

Percentage Vital Capacity Calculated from Body Surface

Men

After MYERS, J. A., *Vital Capacity of the Lungs*, Baltimore, 1925

The body surface is calculated from the weight and height using the DUBOIS formula (see nomogram on page 250), and the vital capacity measured in cubic centimetres. The percentage vital capacity with respect to the ideal value can then be found from the table below.

Body surface in m ²	Vital capacity (cubic centimetres)																															
	600	700	800	900	1000	1100	1200	1300	1400	1500	1600	1700	1800	1900	2000	2100	2200	2300	2400	2500	2600	2700	2800	2900	3000	3100	3200					
0.7	34	40	46	51	57	63	69	74	80	86	92	97	103	108	114	120	125															
0.75	32	37	43	48	53	59	64	69	75	80	85	91	96	101	107	112	117	123														
0.8	30	35	40	45	50	55	60	65	70	75	80	85	90	95	100	105	110	115	120	125												
0.85	28	33	38	42	47	52	57	61	66	71	75	80	85	90	94	99	104	107	113	118	122											
0.9	27	31	35	40	44	49	53	58	62	67	71	76	80	85	89	93	98	102	107	111	115	120										
0.95	25	29	34	38	42	46	51	55	59	63	67	72	76	80	84	88	93	97	101	105	109	114	118	122								
1.0	24	28	32	36	40	44	48	52	56	60	64	68	72	76	80	84	88	92	96	100	104	109	112	116	120							
1.05	23	27	30	34	38	42	46	50	53	57	61	65	69	72	76	80	84	88	91	95	99	103	107	110	114	118	122					
1.1	22	25	29	33	36	40	44	47	51	55	58	62	65	69	73	76	80	84	87	91	95	98	102	105	109	113	116					
1.15	21	24	28	31	35	38	42	45	49	52	56	59	63	66	70	73	77	80	84	87	91	94	98	101	104	108	111					
1.2	20	23	27	30	33	37	40	43	47	50	53	57	60	64	69	70	73	77	80	83	87	90	93	97	100	103	107					
1.25		22	26	29	32	35	38	42	45	48	51	54	58	61	64	67	70	74	77	80	83	86	90	93	96	99	102					
1.3		22	25	28	31	34	37	40	43	46	49	52	55	59	62	65	68	71	74	77	80	83	86	89	92	95	99					
1.35		21	24	27	30	33	36	39	42	44	47	50	53	56	59	62	65	68	71	74	77	80	83	86	89	92	95					
1.4		20	23	26	29	31	34	37	40	43	46	49	51	54	57	60	63	66	69	72	74	77	80	83	86	89	91					
1.45			22	25	28	30	33	36	39	41	44	47	50	52	55	58	61	64	66	69	72	75	77	80	83	86	88					
1.5			21	24	27	29	32	35	37	40	43	45	48	51	53	56	59	61	64	67	69	72	75	77	80	83	85					
1.55			20	23	26	28	31	34	36	39	41	44	46	49	52	54	57	59	62	65	67	70	72	75	77	80	83					
1.6			20	22	25	28	30	33	35	38	40	43	45	48	50	53	55	58	60	63	65	68	70	73	75	78	80					
1.65				22	24	27	29	32	34	36	39	41	44	46	49	51	53	56	58	61	63	66	68	70	73	75	78					
1.7				21	24	26	28	31	33	35	38	40	43	45	47	50	52	54	57	59	61	64	66	68	71	73	75					
1.75				21	23	25	27	30	32	34	37	39	41	43	46	48	50	53	55	57	60	62	64	66	69	71	73					
1.8				20	22	24	27	29	31	33	36	38	40	42	44	47	49	51	53	56	58	60	62	65	67	69	71					
1.85					22	24	26	28	30	32	35	37	39	41	43	45	48	50	52	54	56	58	61	63	65	67	69					
1.9					21	23	25	27	30	32	34	36	38	40	42	44	46	48	51	53	55	57	59	61	63	65	68					
1.95					20	23	25	27	29	31	33	35	37	39	41	43	45	47	49	51	53	55	58	60	62	64	66					
2.0					20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52	54	56	58	60	62	64					
2.05						22	23	25	27	29	31	33	35	37	39	41	43	45	47	49	51	53	55	57	59	60	62					
2.1						21	23	25	27	29	31	32	34	36	38	40	42	44	46	48	50	51	53	55	57	59	61					
2.15						21	22	24	26	28	30	32	34	36	37	39	41	43	45	47	48	50	52	54	56	58	60					
2.2					20	22	24	25	27	29	31	33	35	36	38	40	42	44	46	47	49	51	53	55	56	58	58					
2.25						21	23	25	27	28	30	32	34	36	37	39	41	43	45	46	48	50	52	54	55	57	57					
2.3							21	23	24	26	28	30	31	33	35	37	38	40	42	44	45	47	49	50	52	54	56					
2.35							20	22	24	26	27	29	31	32	34	36	37	39	41	43	44	46	48	49	51	53	54					
2.4							20	22	23	25	27	28	30	32	33	35	37	38	40	42	43	45	47	48	50	52	53					
2.45								21	23	25	26	28	29	31	33	34	36	38	39	41	42	44	46	47	49	51	52					
2.5								21	22	24	26	27	29	30	32	34	35	37	38	40	42	43	45	46	48	50	51					
	3300	3400	3500	3600	3700	3800	3900	4000	4100	4200	4300	4400	4500	4600	4700	4800	4900	5000	5100	5200	5300	5400	5500	5600	5700	5800	5900					
0.7																																
0.75																																
0.8																																
0.85																																
0.9																																
0.95																																
1.0																																
1.05																																
1.1	120	123																														
1.15	115	118	122																													

After MYERS, J. A., *Vital Capacity of the Lungs*, Baltimore, 1925

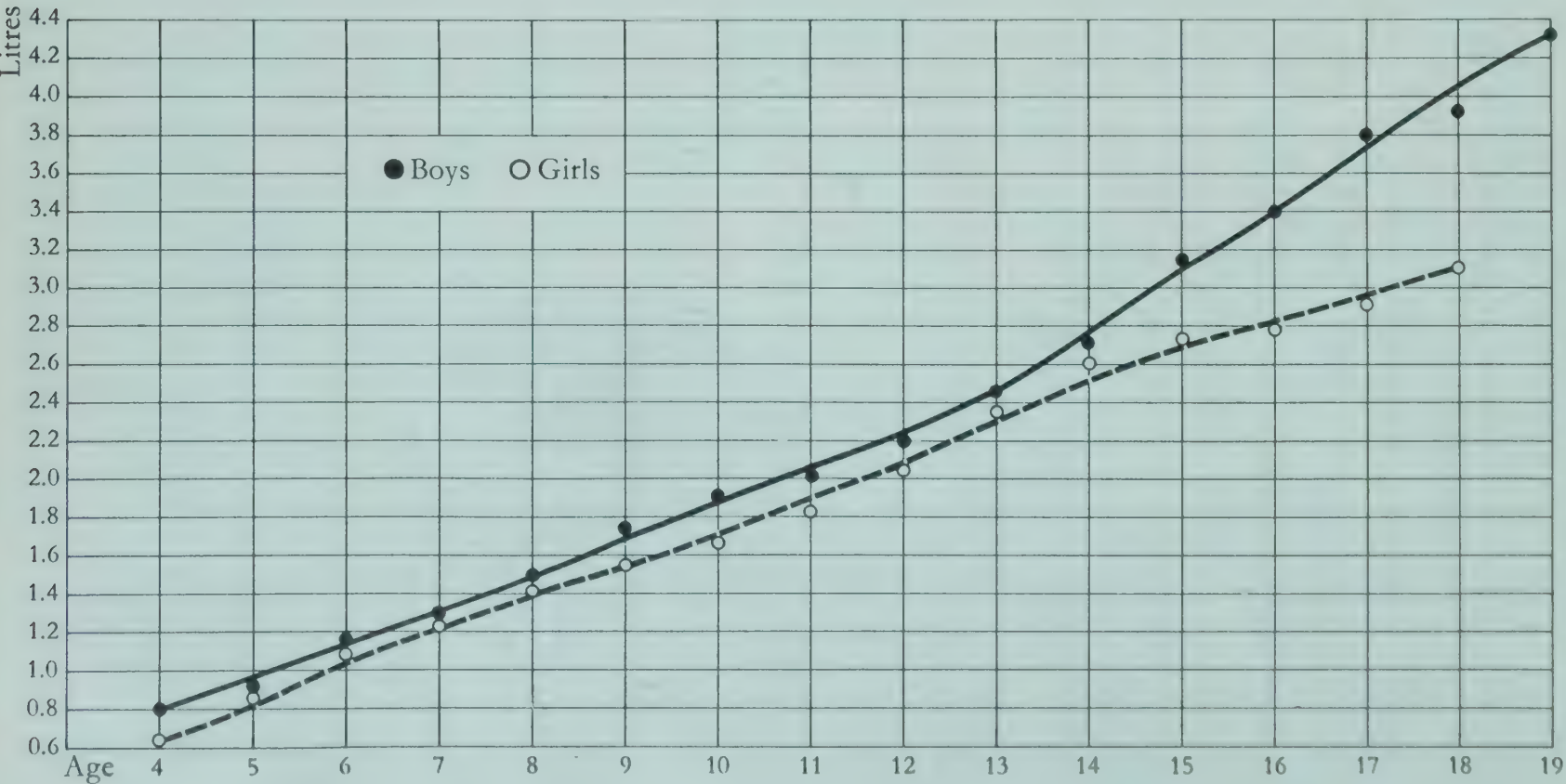
The body surface is calculated from the weight and height using the DUBOIS formula (see nomogram on page 250), and the vital capacity measured in cubic centimetres. The percentage vital capacity with respect to the ideal value can then be found from the table below.

Body surface in m²	Vital capacity (cubic centimetres)																								
	400	500	600	700	800	900	1000	1100	1200	1300	1400	1500	1600	1700	1800	1900	2000	2100	2200	2300	2400	2500			
0.5	42	52	63	73	84	94	104	115	125																
0.55	38	47	57	66	76	85	95	104	114	123															
0.6	35	43	52	61	69	78	87	95	104	113	122														
0.65	32	40	48	56	64	72	80	88	96	104	112	120													
0.7	30	37	45	52	60	67	75	82	90	97	104	112	119	127											
0.75	28	35	42	49	56	63	69	76	83	90	97	104	111	118	125										
0.8	26	33	39	46	52	59	65	72	78	85	91	98	104	111	117	124									
0.85	25	31	37	43	49	55	61	67	74	80	86	92	98	104	110	116	123								
0.9	23	29	35	40	46	52	58	64	69	73	81	87	93	98	104	110	116	122							
0.95	22	27	33	38	44	49	55	60	66	71	77	82	88	93	99	104	110	115	121	126					
1.0	21	26	31	37	42	47	52	57	63	68	73	78	83	89	94	99	104	109	115	120	125				
1.05	20	25	30	35	40	45	50	55	60	64	69	74	79	84	89	94	99	104	109	114	119	124			
1.1		24	28	33	38	43	47	52	57	62	66	71	76	80	85	90	95	99	104	109	113	118			
1.15		23	27	32	36	41	45	50	54	59	63	68	72	77	81	86	91	95	100	104	109	113			
1.2		22	26	30	35	39	43	48	52	56	61	65	69	74	78	83	87	91	96	100	104	108			
1.25		21	25	29	33	37	42	46	50	54	58	63	67	71	75	79	83	88	92	96	100	104			
1.3		20	24	28	32	36	40	44	48	52	56	60	64	68	72	76	80	84	88	92	96	100			
1.35			23	27	31	35	39	42	46	50	54	58	62	66	70	73	77	81	85	89	93	97			
1.4			22	26	30	33	37	41	45	48	52	56	60	63	67	71	74	78	82	86	89	93			
1.45			22	25	29	32	36	40	43	47	50	54	57	61	65	68	72	75	79	83	86	90			
1.5			21	24	28	31	35	38	42	45	49	52	56	59	63	66	69	73	76	80	83	87			
1.55			20	23	27	30	34	37	40	44	47	50	54	57	60	64	67	70	74	77	81	84			
1.6			20	23	26	29	33	36	39	42	46	49	52	55	59	62	65	68	72	75	78	81			
1.65				22	25	28	32	35	38	41	44	47	51	54	57	60	63	66	69	73	76	79			
1.7				21	25	28	31	34	37	40	43	46	49	52	55	58	61	64	67	70	74	77			
1.75				21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	66	68	71	74			
1.8				20	23	26	29	32	35	38	40	43	46	49	52	55	58	61	64	66	69	72			
1.85				20	23	25	28	31	34	37	40	42	45	48	51	54	56	59	62	65	68	70			
1.9					22	25	27	30	33	36	38	41	44	47	49	52	55	58	60	63	66	69			
1.95					21	24	27	29	32	35	37	40	43	45	48	51	53	56	59	61	64	67			
2.0					21	23	26	29	31	34	36	39	42	44	47	50	52	55	57	60	63	65			
2.05					20	23	25	28	31	33	36	38	41	43	46	48	51	53	56	58	61	64			
2.1					20	22	25	27	30	32	35	37	40	42	45	47	50	52	55	57	60	62			
2.15						22	24	26	29	31	34	36	39	41	44	46	48	51	53	56	58	61			
2.2						21	24	26	28	31	33	36	38	40	43	45	47	50	52	54	57	59			
2.25						21	23	25	28	30	32	35	37	39	42	44	46	49	51	53	56	58			
2.3						20	23	25	27	29	32	34	36	39	41	43	45	48	50	52	54	57			
2.35						20	22	24	27	29	31	33	35	38	40	42	44	47	49	51	53	55			
2.4						20	22	24	26	28	30	33	35	37	39	41	43	46	48	50	52	54			
	2600	2700	2800	2900	3000	3100	3200	3300	3400	3500	3600	3700	3800	3900	4000	4100	4200	4300	4400	4500	4600				
0.5																									
0.55																									
0.6																									
0.65																									
0.7																									
0.75																									
0.8																									
0.85																									
0.9																									
0.95																									
1.0																									
1.05																									
1.1	123																								
1.15	118	122																							
1.2	113	117	122																						
1.25	108	113	117	121																					
1.3	104	108	112	116	120	124																			
1.35	100	104	107	112	116	120	123																		

Increase of vital capacity in boys and girls¹

Normal boys									
Age in years	Number of individuals tested	Average height		Vital capacity					
		in.	cm	Average ccm	Minimum ccm	Maximum ccm	Probable error ccm	Standard deviation σ ccm	Variation coefficient %
4	6	40.7	103.4	792	500	900			
5	20	42.0	106.8	927	600	1150			
6	62	44.2	112.2	1154	800	1600	15.6	182	15.8
7	112	46.0	116.9	1290	900	2200	12.3	194	15.0
8	98	48.0	121.8	1468	1050	2100	15.0	220	15.0
9	110	51.1	129.9	1715	1200	2300	15.8	246	14.3
10	87	52.5	133.4	1872	1400	2650	18.9	262	14.0
11	113	54.2	137.8	1991	1300	2800	17.1	270	13.6
12	114	56.1	142.4	2182	1300	3300	21.5	340	15.6
13	132	58.5	148.7	2458	1700	4000	25.2	430	17.5
14	177	60.9	154.8	2712	1400	4300	24.5	484	17.8
15	155	63.0	159.9	3145	1850	4400	29.8	551	17.5
16	67	65.8	167.2	3425	2100	4300	47.2	573	16.7
17	23	67.5	171.4	3776	2400	4500			
18	9	67.7	172.0	3922	2750	4400			
19	4	66.2	168.2	4300	4100	4500			

Normal girls									
4	9	37.6	95.4	664	350	850			
5	26	41.8	106.4	888	600	1200			
6	62	43.8	111.5	1085	700	1600	14.0	163	15.0
7	81	45.0	114.4	1228	900	1800	13.6	181	14.7
8	76	47.6	121.0	1401	800	1950	15.4	199	13.5
9	73	50.0	127.0	1513	1000	2250	18.1	229	15.1
10	117	52.1	132.1	1672	900	2400	17.0	273	16.3
11	119	53.5	135.9	1799	1250	2550	14.9	241	13.4
12	135	56.7	144.0	2053	1400	2900	19.9	343	16.7
13	162	59.6	151.4	2349	1550	3600	21.7	409	17.5
14	192	61.6	156.6	2607	1900	3800	17.5	361	13.9
15	131	62.2	157.8	2702	1900	3700	24.3	413	15.3
16	29	63.1	160.1	2778	2050	3500			
17	7	64.0	162.6	2943	2250	3400			
18	1	63.8	162.0	3100					



¹) After STEWART and SHEETS, *Am. J. Dis. Child.*, 24, 83,451, 1922.

(15–30 years, weight without clothing)

The table gives three weights for each height: 1. Average weight for persons of medium build (**bold figures**). 2. Average weight for persons of light build (above the bold figures). 3. Average weight for persons of heavy build (below the bold figures).

Formulae for normal weight

According to BROCA: Ideal weight in kg = height in centimetres minus 100.
According to BORNHARDT: $\text{Ideal weight in kg} = \frac{\text{height in cm} \times \text{average chest measurement in cm}}{240}$

Women										Men									
Height		Weight								Height		Weight							
ft. in.	cm	15 years		20 years		25 years		30 years ²		ft. in.	cm	15 years		20 years		25 years		30 years ²	
		lb.	kg	lb.	kg	lb.	kg	lb.	kg			lb.	kg	lb.	kg	lb.	kg	lb.	kg
4 8	142.5	90	40.8	95	43.0	97	44.0	100	45.3	4 11	150	92	41.7	101	45.8	105	47.6	109	49.4
		100	45.3	105	47.6	108	49.0	111	50.3			102	46.2	112	50.7	117	53.0	121	54.8
		113	51.2	117	53.0	122	55.3	125	56.6			114	51.6	126	57.1	131	59.3	136	61.6
4 9	145	91	41.2	96	43.5	99	44.8	102	46.2	5 0	152.5	94	42.6	103	46.7	107	48.5	111	50.3
		101	45.8	107	48.5	110	49.8	113	51.2			104	47.1	114	51.6	119	53.9	123	55.7
		114	51.6	119	53.9	124	56.2	127	57.5			117	53.0	128	58.0	134	60.7	138	62.5
4 10	147.5	92	41.7	98	44.4	101	45.8	104	47.1	5 1	155	96	43.5	105	47.6	109	49.4	113	51.2
		102	46.2	109	49.4	112	50.7	115	52.1			107	48.5	117	53.0	121	54.8	125	56.6
		115	52.1	123	55.7	126	57.1	129	58.4			120	54.4	131	59.3	136	61.6	140	63.4
4 11	150	94	42.6	100	45.3	103	46.7	105	47.6	5 2	157.5	99	44.9	108	48.9	112	50.7	115	52.1
		104	47.1	111	50.3	114	51.6	117	53.0			110	49.8	120	54.4	124	56.2	128	58.0
		117	53.0	125	56.6	128	58.0	132	59.8			124	56.2	135	61.2	139	63.0	144	65.2
5 0	152.5	96	43.5	103	46.7	104	47.1	107	48.5	5 3	160	102	46.2	111	50.3	115	52.1	118	53.5
		107	48.5	114	51.6	116	52.6	119	53.9			113	51.2	123	55.7	128	58.0	131	59.3
		120	54.4	128	58.0	131	59.3	134	60.7			127	57.5	138	62.5	144	65.2	147	66.6
5 1	155	99	44.8	105	47.6	107	48.5	110	49.8	5 4	162.5	105	47.6	114	51.6	119	53.9	122	55.3
		110	49.8	117	53.0	119	53.8	122	55.3			117	53.0	127	57.5	132	59.8	135	61.2
		122	55.3	132	59.8	134	60.7	137	62.1			131	59.3	143	64.8	148	67.0	152	68.9
5 2	157.5	102	46.2	108	48.9	111	50.3	113	51.2	5 5	165	109	49.4	118	53.5	123	55.7	125	56.6
		113	51.2	120	54.4	123	55.7	125	56.6			121	54.8	131	59.3	136	61.6	139	63.0
		127	57.5	135	61.2	138	62.5	141	63.9			136	61.6	147	66.6	153	69.3	156	70.7
5 3	160	104	47.1	111	50.3	113	51.2	116	52.5	5 6	167.5	113	51.2	122	55.3	126	57.1	129	58.4
		116	52.5	123	55.9	126	57.1	129	58.4			125	56.6	135	61.2	140	63.4	143	64.8
		131	59.3	138	62.5	142	64.3	145	65.7			140	63.4	152	68.9	157	71.1	161	72.9
5 4	162.5	108	48.9	113	51.2	116	52.5	119	53.9	5 7	170	116	52.5	125	56.6	130	58.9	132	59.8
		120	54.4	126	57.1	129	58.4	132	59.8			129	58.4	139	63.0	144	65.2	147	66.6
		135	61.2	142	64.3	145	65.7	149	67.5			145	65.7	156	70.7	162	73.4	165	74.7
5 5	165	112	50.7	117	53.0	120	54.4	123	55.7	5 8	172.5	120	54.4	129	58.4	133	60.2	136	61.6
		124	56.2	130	58.9	133	60.2	136	61.6			133	60.2	143	64.8	148	67.0	151	68.4
		140	63.4	146	66.1	149	67.5	153	69.3			149	67.5	161	73.0	166	75.2	170	77.0
5 6	167.5	115	52.1	121	54.9	123	55.7	126	57.1	5 9	175	123	55.7	132	59.8	137	62.1	141	63.9
		128	58.0	134	60.7	137	62.1	140	63.4			137	62.1	147	66.6	152	68.9	156	70.7
		144	65.2	151	68.4	154	69.8	158	71.6			154	69.8	165	74.7	171	77.5	175	79.3
5 7	170	119	53.9	124	56.2	127	57.5	130	58.9	5 10	177.5	128	58.0	136	61.6	141	63.9	145	65.7
		132	59.8	138	62.5	141	63.9	144	65.2			142	64.3	151	68.4	157	71.1	161	72.9
		149	67.5	155	70.2	158	71.6	162	73.4			159	72.0	170	77.0	176	79.7	181	82.0
5 8	172.5	122	55.3	127	57.5	131	59.3	133	60.2	5 11	180	132	59.8	141	63.9	146	66.1	150	68.0
		136	61.6	141	63.9	145	65.7	148	67.0			147	66.6	156	70.7	162	73.4	167	75.7
		153	69.3	159	72.0	163	73.8	167	75.7			165	74.7	175	79.3	182	82.4	188	85.2
5 9	175	126	57.1	131	59.3	134	60.7	136	61.6	6 0	183	137	62.1	145	65.7	151	68.4	156	70.7
		140	63.4	145	65.7	149	67.5	151	68.4			152	68.9	161	72.9	168	76.1	173	78.4
		158	71.6	163	73.8	167	75.7	170	77.0			171	77.5	181	82.0	189	85.6	194	87.9
5 10	178	131	59.3	134	60.7	137	62.1	140	63.4	6 1	185.5	141	63.9	150	68.0	157	71.1	161	72.9
		145	65.7	149	67.5	152	68.9	155	70.2			157	71.1	166	75.2	174	78.8	179	81.1
		163	73.9	168	76.1	171	77.5	174	78.9			176	79.7	186	84.3	195	88.3	201	91.1
5 11	180	135	61.2	139	63.0	140	63.4	143	64.8	6 2	188	146	66.1	154	69.8	161	73.0	167	75.7
		150	68.0	154	69.8	156	70.7	159	72.0			162	73.4	171	77.5	179	81.1	185	83.8
		168	76.1	173	78.4	176	79.7	179	81.1			182	82.4	192	87.0	201	91.1	208	94.2

¹) Table from Life Extension Institute of New York City.
²) The ideal weight for 30 years should be maintained throughout life.

The arithmetical mean of the values of a particular measurement made on a large number of individuals is usually accepted as the *normal measurement*, or *norm*. In practice, however, this figure is often found to be inadequate since it does not necessarily take into account the question of the normality of deviations. For this reason it is becoming increasingly the practice to supplement it by the standard deviation σ (see page 32), the two figures together defining the normal range of the values without ambiguity (mean $\pm 2\sigma$).

The extraction of data from growth tables based on means and standard deviations, however, involves tedious calculation. This can be avoided by using tables based on the *percentile division* of the normal distribution curve (GAUSS or GALTON curve). Such tables make it possible, on a statistically reliable basis,

1.

to assess values deviating from the mean,
2.

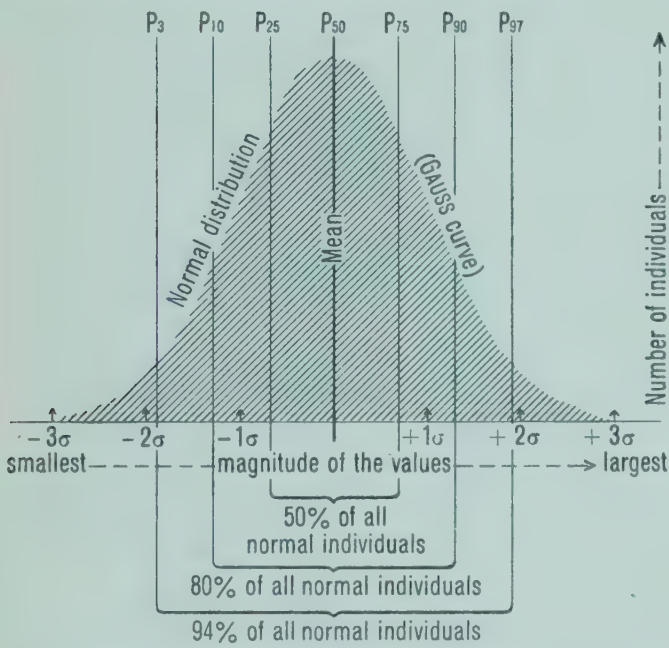
to allocate an individual subject to a particular category by means of a simple index,
3.

to define various normal ranges according to requirements.

In the percentile division of the normal distribution curve the latter is divided by 7 zonal lines designated P_3 , P_{10} , P_{25} , P_{50} , P_{75} , P_{90} and P_{97} . The magnitude of the normal values increases in the direction P_3 – P_{97} , the smallest values being on the left and the largest on the right. The P-indices serve to indicate the limiting magnitudes which divide the total number of observed measurements of normal individuals into classes, as follows:

P_3	3% of all normal individual values are smaller, 97% are greater
P_{10}	10% of all normal individual values are smaller, 90% are greater
P_{25}	25% of all normal individual values are smaller, 75% are greater
P_{50}	50% of all normal individual values are smaller, 50% are greater, etc.

P_{50} is at the same time the mean of all normal values and coincides with the zero point of the normal distribution.



With the aid of these tables the value for any individual is conveniently designated by the appropriate P-index and the actual numerical value may be disregarded.

Examples: Boys aged 3 months:

(a)	weight 11.6 lb.	weight index P 25–
(b)	weight 11.8 lb.	weight index P 25
(c)	weight 12.0 lb.	weight index P 25+
(d)	weight 12.2 lb.	weight index P 25–50
etc.		

or, if great accuracy is unnecessary

(a)	{	weight index P 25
(b)			
(c)			
(d)			
etc.			

If now in the case of (b), for example, all the body measurements are in the neighbourhood of P_{25} it can be assumed that the child is normally developed and belongs for the time being to the 25% group of smaller-than-normal individuals of this particular age. If

the child retains the same P-index throughout his growth, then the latter is also to be regarded as normal, i.e. the child belongs definitely to the 25% group of smaller individuals.

Anomalies in the relation between particular body measurements (e.g. weight:height, height:chest measurement, etc.) are made immediately obvious by the P-indices, without the necessity of calculation.

Example. Girl aged 6 months.			
Weight	14.3 lb.	Index: P 10 +	The average index is about P_{50} and the child should be put in this class. Bearing in mind <i>all</i> the body measurements (not only height or weight) it should be regarded as normally developed, but much under weight.
Length	26 in.	P 50–75	
Pelvic breadth	4.4 in.	P 50	
Head circumference	16.7 in.	P 50–	
Chest circumference	17.0 in.	P 50+	
Abdominal circumference	15.4 in.	P 25–	

Furthermore, the percentile division makes it possible to divide values into groups according to their greater or smaller *probability of normality*. Various possibilities can be taken into consideration, according to requirements.

Thus 94% of the values for all normal individuals lie between the limits P_3 and P_{97} (mathematically expressed: if a large number of normal individuals are measured, 94% of the values can be expected to fall within this range). This range coincides fairly closely with the generally accepted normal range (mean $\pm 2\sigma$). The values for 50% of all normal individuals lie between P_{25} and P_{75} (distributed symmetrically about the mean), and so on. In order to calculate these ranges it is only necessary to subtract the smaller P-index from the greater, giving the percentage of normal individuals falling inside these limits, e.g. P_{75} – P_{25} = 50%. Unsymmetrical ranges can also be calculated if desired, i.e. considering only the values smaller or greater than the mean.

The tables are based on the measurements of two groups of children of almost exclusively western European descent in the USA. The two groups cover respectively the periods birth–5 years and 5–18 years. The values for sitting height are from a separate investigation. All weight values are expressed both in pounds and kilograms, and all length or height values in inches and centimetres. In order to simplify presentation, pounds and inches are given to the first decimal place. Values expressed in *metric units* are printed in *italics* throughout.

Birth—9 Months

(Weights are in pounds and *kilograms*, length measurements in inches and *centimetres*)

Boys

Girls

94% of the values for all normal individuals							Birth	94% of the values for all normal individuals							
80% of all values						80% of all values									
50% of all values						50% of all values									
P ₃	P ₁₀	P ₂₅	Mean P ₅₀	P ₇₅	P ₉₀	P ₉₇		P ₃	P ₁₀	P ₂₅	Mean P ₅₀	P ₇₅	P ₉₀	P ₉₇	
5.8 2.63	6.3 2.86	6.9 3.13	7.5 3.4	8.3 3.76	9.1 4.13	10.1 4.58	Weight	5.8 2.63	6.2 2.81	6.9 3.13	7.4 3.36	8.1 3.67	8.6 3.9	9.4 4.26	
18.2 46.3	18.9 48.1	19.4 49.3	19.9 50.6	20.5 52.0	21.0 53.3	21.5 54.6	Length	18.5 47.1	18.8 47.8	19.3 49.0	19.8 50.2	20.1 51.0	20.4 51.9	21.1 53.6	
2.8 7.1	2.9 7.4	3.0 7.7	3.2 8.1	3.3 8.4	3.4 8.7	3.5 9.0	Pelvic breadth	2.8 7.0	2.8 7.2	2.9 7.4	3.0 7.7	3.2 8.2	3.3 8.5	3.5 8.9	
13.0 33.0	13.2 33.5	13.5 34.4	13.9 35.3	14.3 36.2	14.6 37.0	14.8 37.5	Head circ.	12.8 32.5	13.1 33.4	13.3 33.9	13.7 34.7	13.9 35.4	14.2 36.0	14.4 36.6	
11.7 29.8	12.1 30.6	12.5 31.8	13.1 33.2	13.5 34.4	14.1 35.7	14.5 36.8	Chest circ.	11.8 30.0	12.1 30.8	12.5 31.8	12.9 32.9	13.4 34.0	13.8 35.0	14.2 36.0	
3 Months							3 Months	3 Months							
10.6 4.81	11.1 5.03	11.8 5.35	12.6 5.72	13.6 6.17	14.5 6.58	16.4 7.44		Weight	9.8 4.45	10.7 4.85	11.4 5.17	12.4 5.62	13.2 5.99	14.0 6.35	14.9 6.76
22.4 56.8	22.8 57.8	23.3 59.3	23.8 60.4	24.3 61.8	24.7 62.8	25.1 63.7		Length	22.0 55.8	22.4 56.9	22.8 57.9	23.4 59.5	23.9 60.7	24.3 61.7	24.8 63.1
3.9 9.8	3.9 10.0	4.0 10.2	4.2 10.6	4.4 11.2	4.5 11.5	4.8 12.1		Pelvic breadth	3.7 9.4	3.8 9.6	3.9 9.9	4.1 10.4	4.3 10.9	4.5 11.4	4.8 12.2
15.2 38.7	14.9 39.2	15.7 40.0	16.1 40.9	16.4 41.5	16.6 42.1	17.0 43.2		Head circ.	14.9 37.9	15.2 38.5	15.4 39.2	15.7 40.0	16.1 40.8	16.4 41.7	16.7 42.3
14.8 37.6	15.1 38.3	15.5 39.3	16.0 40.6	16.4 41.6	16.9 42.9	17.4 44.1		Chest circ.	14.4 36.5	14.8 37.6	15.3 38.8	15.7 39.8	16.1 40.9	16.5 42.0	16.9 43.0
13.3 33.6	14.0 35.5	14.5 36.8	15.2 38.5	15.7 39.8	16.3 41.4	17.1 43.5		Abdominal circ.	12.7 32.3	13.5 34.4	14.5 36.8	15.1 38.4	15.9 40.4	16.4 42.7	16.8 42.7
6 Months							6 Months	6 Months							
14.0 6.35	14.8 6.71	15.6 7.08	16.7 7.58	18.0 8.16	19.2 8.71	20.8 9.43		Weight	12.7 5.76	14.1 6.4	15.0 6.8	16.0 7.26	17.5 7.94	18.6 8.44	20.0 9.07
24.8 63.0	25.2 63.9	25.7 65.2	26.1 66.4	26.7 67.8	27.3 69.3	27.7 70.4		Length	24.0 61.1	24.6 62.5	25.1 63.7	25.7 65.2	26.2 66.6	26.7 67.8	27.1 68.8
16.3 41.4	16.7 42.3	17.1 43.4	17.7 44.8	18.2 46.2	18.7 47.4	19.1 48.4		Sitting height	15.8 40.0	16.1 41.0	16.6 42.1	17.1 43.3	17.5 44.5	18.0 45.6	18.3 46.8
4.1 10.5	4.3 10.8	4.4 11.2	4.6 11.6	4.7 12.0	4.9 12.4	5.2 13.1		Pelvic breadth	4.1 10.3	4.1 10.5	4.3 10.8	4.4 11.3	4.6 11.8	4.9 12.4	5.2 13.2
16.6 42.1	16.8 42.7	17.1 43.3	17.3 43.9	17.6 44.8	17.8 45.4	18.1 45.9		Head circ.	16.1 40.9	16.3 41.4	16.5 42.0	16.8 42.8	17.2 43.6	17.5 44.5	17.9 45.4
15.8 40.1	16.4 41.6	16.7 42.5	17.2 43.7	17.7 45.0	18.2 46.3	18.6 47.2		Chest circ.	15.5 39.4	16.0 40.6	16.4 41.8	16.9 43.0	17.4 44.2	17.9 45.4	18.4 46.6
14.3 36.4	15.1 38.4	15.7 39.8	16.3 41.4	17.0 43.2	17.7 45.0	18.1 46.0	Abdominal circ.	14.3 36.2	14.9 37.9	15.5 39.5	16.3 41.4	17.1 43.5	17.7 45.0	18.2 46.2	
9 Months							9 Months	9 Months							
16.6 7.53	17.8 8.07	18.7 8.48	20.0 9.07	21.5 9.75	22.9 10.39	24.4 11.07		Weight	15.1 6.85	16.6 7.53	17.8 8.03	19.2 8.71	20.8 9.43	22.4 10.16	24.2 10.98
26.6 67.7	27.0 68.6	27.5 69.8	28.0 71.2	28.7 72.9	29.2 74.2	29.9 75.9		Length	25.7 65.4	26.4 67.0	26.9 68.4	27.6 70.1	28.2 71.7	28.7 72.9	29.2 74.1
4.3 11.0	4.5 11.5	4.7 11.9	4.8 12.3	5.0 12.7	5.2 13.1	5.4 13.7		Pelvic breadth	4.3 11.0	4.4 11.3	4.5 11.5	4.7 12.0	4.9 12.5	5.2 13.1	5.4 13.8
17.3 43.8	17.5 44.5	17.8 45.1	18.1 46.0	18.3 46.5	18.5 47.1	18.8 47.8		Head circ.	16.8 42.6	17.0 43.2	17.3 43.8	17.6 44.6	17.9 45.4	18.2 46.3	18.6 47.2
16.5 42.0	17.2 43.7	17.7 44.8	18.1 46.0	18.7 47.5	19.3 48.9	19.7 49.9		Chest circ.	16.4 41.7	16.8 42.7	17.3 44.0	17.9 45.4	18.3 46.6	18.9 47.9	19.4 49.2
15.0 38.1	15.8 40.1	16.4 41.7	17.1 43.4	18.0 45.6	18.7 47.6	19.1 48.4		Abdominal circ.	15.0 38.0	15.7 39.9	16.3 41.3	17.1 43.4	18.0 45.7	18.8 47.7	19.4 49.2

¹) Quoted by STUART, H. C., and STEVENSON, S. S., *Physical Growth and Development*, in NELSON, *Mitchell-Nelson Textbook of Pediatrics*, Philadelphia, 1950.

Boys

Girls

94% of the values for all normal individuals								94% of the values for all normal individuals						
80% of all values								80% of all values						
50% of all values								50% of all values						
Mean								Mean						
P ₃	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₇		P ₃	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₇
							12 Months							
18.5 8.39	19.6 8.89	20.9 9.48	22.2 10.07	23.8 10.8	25.4 11.52	27.3 12.38	Weight	16.8 7.62	18.4 8.35	19.8 8.98	21.5 9.75	23.0 10.43	24.8 11.25	27.1 12.29
28.1 71.3	28.5 72.4	29.0 73.7	29.6 75.2	30.3 76.9	30.7 78.1	31.6 80.3	Length	27.1 68.9	27.8 70.6	28.5 72.3	29.2 74.2	29.9 75.9	30.3 77.1	31.0 78.8
17.8 45.1	18.1 46.1	18.7 47.4	19.2 48.7	19.7 50.1	20.4 51.2	20.6 52.4	Sitting height	17.4 44.2	17.8 45.2	18.2 46.3	18.7 47.5	19.2 48.7	19.6 49.8	20.0 50.9
4.5 11.4	4.7 11.9	4.9 12.4	5.0 12.8	5.2 13.2	5.4 13.7	5.6 14.2	Pelvic breadth	4.5 11.4	4.6 11.7	4.7 12.0	4.9 12.4	5.1 13.0	5.4 13.6	5.7 14.4
17.7 44.9	17.9 45.5	18.3 46.5	18.6 47.3	18.8 47.8	19.1 48.4	19.3 48.9	Head circ.	17.2 43.6	17.4 44.3	17.7 45.0	18.0 45.8	18.4 46.7	18.8 47.7	19.0 48.4
17.1 43.5	17.8 45.1	18.2 46.3	18.7 47.6	19.4 49.3	20.0 50.7	20.4 51.9	Chest circ.	17.0 43.1	17.4 44.2	17.9 45.6	18.5 47.0	19.0 48.2	19.5 49.5	20.0 50.9
15.5 39.3	16.2 41.1	16.9 42.9	17.5 44.6	18.5 47.0	19.2 48.9	19.7 50.0	Abdominal circ.	15.2 38.7	16.1 40.9	16.7 42.4	17.5 44.5	18.1 46.9	19.4 49.2	20.1 51.1
							15 Months							
19.8 8.98	21.0 9.53	22.4 10.16	23.7 10.75	25.4 11.52	27.2 12.34	29.4 13.33	Weight	18.1 8.21	19.8 8.98	21.3 9.66	23.0 10.43	24.6 11.16	26.6 12.07	29.0 13.15
29.3 74.4	29.8 75.6	30.3 77.0	30.9 78.5	31.6 80.3	32.1 81.5	33.1 84.2	Length	28.3 71.9	29.0 73.7	29.8 75.6	30.5 77.6	31.3 79.4	31.8 80.8	32.6 82.8
4.6 11.8	4.9 12.4	5.0 12.8	5.2 13.3	5.4 13.7	5.6 14.2	5.8 14.7	Pelvic breadth	4.6 11.6	4.8 12.1	4.9 12.4	5.1 12.9	5.3 13.5	5.6 14.1	5.8 14.8
18.0 45.6	18.2 46.3	18.5 47.1	18.8 48.0	19.1 48.5	19.4 49.2	19.6 49.8	Head circ.	17.5 44.3	17.7 44.9	18.0 45.6	18.3 46.5	18.7 47.4	19.1 48.4	19.3 49.1
17.6 44.7	18.2 46.1	18.6 47.3	19.1 48.6	19.7 50.1	20.4 51.7	20.8 52.8	Chest circ.	17.4 44.1	17.8 45.1	18.3 46.5	18.9 47.9	19.4 49.2	19.9 50.5	20.4 51.9
15.8 40.0	16.4 41.7	17.1 43.5	17.8 45.1	18.7 47.4	19.4 49.3	19.9 50.5	Abdominal circ.	15.5 39.3	16.3 41.5	16.9 43.0	17.7 45.0	18.6 47.3	19.6 49.8	20.4 51.8
							18 Months							
21.1 9.57	22.3 10.12	23.8 10.8	25.2 11.43	26.9 12.2	29.0 13.15	31.5 14.29	Weight	19.4 8.8	21.2 9.62	22.7 10.3	24.5 11.11	26.2 11.88	28.3 12.84	30.9 14.02
30.5 77.5	31.0 78.8	31.6 80.3	32.2 81.8	32.9 83.7	33.5 85.0	34.7 88.2	Length	29.5 74.9	30.2 76.8	31.1 79.0	31.8 80.9	32.6 82.9	33.3 84.5	34.1 86.7
19.0 48.3	19.4 49.2	19.8 50.3	20.3 51.6	20.8 52.9	21.3 54.1	21.8 55.4	Sitting height	18.6 47.1	19.0 48.1	19.4 49.2	19.8 50.4	20.3 51.6	20.8 52.7	21.2 53.9
4.8 12.1	5.0 12.8	5.2 13.2	5.4 13.7	5.6 14.2	5.8 14.7	6.0 15.2	Pelvic breadth	4.6 11.8	4.9 12.4	5.0 12.8	5.2 13.3	5.5 13.9	5.7 14.5	6.0 15.2
18.2 46.2	18.5 47.0	18.8 47.7	19.2 48.7	19.4 49.2	19.6 49.9	19.9 50.6	Head circ.	17.7 44.9	17.9 45.5	18.2 46.2	18.5 47.1	18.9 48.0	19.3 49.0	19.6 49.8
18.1 45.9	18.5 47.0	19.0 48.2	19.5 49.5	20.0 50.9	20.7 52.6	21.1 53.7	Chest circ.	17.7 45.0	18.1 46.0	18.6 47.3	19.2 48.8	19.7 50.2	20.2 51.4	20.8 52.9
16.0 40.6	16.6 42.2	17.3 44.0	17.9 45.5	18.8 47.8	19.6 49.6	20.0 50.9	Abdominal circ.	15.7 39.8	16.6 42.1	17.2 43.6	17.9 45.5	18.7 47.6	19.8 50.3	20.7 52.5
							2 Years							
23.3 10.57	24.7 11.2	26.3 11.93	27.7 12.56	29.7 13.47	31.9 14.47	34.9 15.83	Weight	21.6 9.8	23.5 10.66	25.3 11.48	27.1 12.29	29.2 13.25	31.7 14.38	34.4 15.6
32.6 82.7	33.1 84.2	33.8 85.8	34.4 87.5	35.2 89.4	35.9 91.1	37.2 94.6	Height	31.5 80.1	32.3 82.0	33.3 84.7	34.1 86.6	35.0 88.9	35.8 91.0	36.7 93.3
19.9 50.6	20.2 51.4	20.7 52.5	21.2 53.8	21.7 55.1	22.2 56.3	22.7 57.6	Sitting height	19.4 49.2	19.7 50.2	20.2 51.4	20.7 52.7	21.2 54.0	21.7 55.2	22.2 56.4
5.0 12.8	5.3 13.5	5.5 13.9	5.7 14.4	5.9 15.0	6.1 15.5	6.3 16.1	Pelvic breadth	4.9 12.5	5.2 13.1	5.3 13.5	5.6 14.1	5.8 14.7	6.0 15.3	6.3 16.1
18.5 47.0	18.9 48.0	19.0 48.2	19.6 49.7	19.8 50.2	20.1 51.0	20.4 51.7	Head circ.	18.0 45.8	18.3 46.4	18.6 47.2	18.9 48.1	19.3 49.1	19.7 50.1	20.0 50.9
18.7 47.4	19.0 48.4	19.5 49.5	20.0 50.8	20.6 52.2	21.2 53.9	21.6 54.9	Chest circ.	18.2 46.3	18.7 47.4	19.1 48.6	19.7 50.1	20.4 51.8	20.9 53.0	21.3 54.2
16.4 41.6	17.1 43.4	17.7 44.8	18.2 46.2	19.0 48.4	19.8 50.2	20.2 51.5	Abdominal circ.	16.0 40.7	16.8 42.8	17.5 44.4	18.2 46.3	19.1 48.5	20.2 51.4	21.1 53.5

¹) Quoted by STUART, H. C., and STEVENSON, S. S., *Physical Growth and Development*, in NELSON, *Mitchell-Nelson Textbook of Pediatrics*, Philadelphia, 1950.

2½—4 Years

(Weights are in pounds and *kilograms*, length measurements in inches and *centimetres*)

Boys

Girls

94% of the values for all normal individuals								94% of the values for all normal individuals							
80% of all values								80% of all values							
50% of all values						50% of all values									
			Mean								Mean				
P ₃	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₇	2½ Years	P ₃	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₇	
25.2	26.6	28.4	30.0	32.2	34.5	37.0	Weight	23.6	25.5	27.4	29.6	31.9	34.6	38.2	
11.43	12.07	12.88	13.61	14.61	15.65	16.78		10.7	11.57	12.43	13.43	14.47	15.69	17.33	
34.2	34.8	35.5	36.3	37.0	37.9	39.2		33.3	34.0	35.2	36.0	36.9	37.9	38.9	
86.9	88.5	90.2	92.1	94.1	96.2	99.5	Height	84.5	86.3	89.3	91.4	93.8	96.4	98.7	
20.5	20.9	21.3	21.9	22.4	22.9	23.4		20.0	20.4	20.9	21.4	21.9	22.4	23.0	
52.2	53.1	54.2	55.6	56.9	58.1	59.5		50.9	51.9	53.1	54.4	55.7	57.0	58.3	
5.4	5.6	5.7	5.9	6.2	6.4	6.6	Sitting height	5.2	5.4	5.6	5.8	6.1	6.3	6.7	
13.6	14.2	14.6	15.1	15.7	16.2	16.7		13.2	13.7	14.2	14.8	15.4	16.1	16.9	
18.7	19.1	19.4	19.8	20.0	20.3	20.6		18.2	18.5	18.8	19.2	19.6	20.0	20.3	
47.5	48.5	49.2	50.2	50.9	51.6	52.3	Head circ.	46.3	47.0	47.8	48.8	49.8	50.8	51.5	
19.0	19.4	19.8	20.4	20.9	21.6	22.0		18.7	19.1	19.6	20.2	20.8	21.4	21.9	
48.2	49.3	50.3	51.7	53.2	54.9	55.8		47.3	48.4	49.7	51.2	52.8	54.3	55.5	
16.6	17.4	18.0	18.4	19.4	20.0	20.5	Chest circ.	16.5	17.2	17.8	18.5	19.5	20.8	21.6	
42.0	44.0	45.5	46.7	49.1	50.7	52.0		41.7	43.6	45.2	47.0	49.4	52.6	54.7	
							Abdominal circ.								
							3 Years								
27.0	28.7	30.3	32.2	34.5	36.8	39.2	Weight	25.6	27.6	29.6	31.8	34.6	37.4	41.8	
12.25	13.02	13.74	14.61	15.65	16.69	17.78		11.61	12.52	13.43	14.42	15.69	16.96	18.96	
35.7	36.3	37.0	37.9	38.8	39.6	40.5		34.8	35.6	36.8	37.7	38.6	39.8	40.7	
90.6	92.3	93.9	96.2	98.5	100.5	102.8	Height	88.4	90.5	93.4	95.7	98.1	101.1	103.5	
21.1	21.5	21.9	22.5	23.1	23.6	24.1		20.6	21.1	21.6	22.1	22.6	23.2	23.7	
53.5	54.5	55.6	57.1	58.5	59.7	61.1		52.2	53.4	54.6	56.0	57.4	58.7	60.0	
5.6	5.8	6.0	6.2	6.5	6.7	6.8	Sitting height	5.4	5.6	5.8	6.1	6.3	6.6	7.0	
14.2	14.8	15.2	15.8	16.4	16.9	17.4		13.8	14.3	14.8	15.4	16.1	16.8	17.7	
18.9	19.3	19.6	19.9	20.2	20.5	20.8		18.5	18.7	19.1	19.4	19.8	20.1	20.5	
47.9	48.9	49.6	50.4	51.3	51.9	52.7	Head circ.	46.8	47.5	48.4	49.3	50.3	51.1	52.0	
19.3	19.7	20.1	20.6	21.3	22.0	22.5		18.9	19.4	19.9	20.5	21.1	21.7	22.4	
48.9	49.9	51.0	52.4	54.1	55.8	57.0		47.9	49.3	50.5	51.9	53.5	55.1	56.7	
16.6	17.6	18.1	18.6	19.6	20.1	20.8	Chest circ.	16.8	17.5	18.1	18.8	19.8	21.1	22.0	
42.1	44.6	46.0	47.2	49.6	51.1	52.7		42.7	44.5	46.0	47.7	50.2	53.6	55.8	
							Abdominal circ.								
							3½ Years								
28.5	30.4	32.3	34.3	36.7	39.1	41.5	Weight	27.5	29.5	31.5	33.9	37.0	40.4	45.3	
12.93	13.79	14.65	15.56	16.65	17.74	18.82		12.47	13.38	14.29	15.38	16.78	18.33	20.55	
37.1	37.8	38.4	39.3	40.3	41.1	41.9		36.2	37.1	38.1	39.2	40.2	41.5	42.5	
94.3	96.0	97.5	99.8	102.5	104.5	106.5	Height	92.0	94.2	96.9	99.5	102.0	105.4	108.0	
21.6	22.0	22.5	23.2	23.7	24.2	24.7		21.2	21.6	22.1	22.7	23.3	23.8	24.3	
54.8	55.8	57.0	58.6	60.0	61.2	62.6		53.6	54.8	56.1	57.5	59.0	60.3	61.6	
5.8	6.0	6.2	6.4	6.7	6.8	7.0	Sitting height	5.7	5.9	6.1	6.3	6.6	6.8	7.2	
14.7	15.3	15.7	16.3	16.9	17.4	17.9		14.4	14.9	15.4	16.0	16.7	17.4	18.3	
19.5	19.9	20.3	20.9	21.6	22.3	22.8		19.1	19.7	20.1	20.6	21.3	22.0	22.9	
49.6	50.5	51.6	53.1	54.9	56.6	58.0	Head circ.	48.5	50.1	51.2	52.5	54.1	55.8	58.1	
							4 Years								
30.1	32.1	34.0	36.4	39.0	41.4	44.3	Weight	29.2	31.2	33.5	36.2	39.6	43.5	48.2	
13.65	14.56	15.42	16.51	17.69	18.78	20.09		13.25	14.15	15.2	16.42	17.96	19.73	21.86	
38.4	39.1	39.7	40.7	41.9	42.7	43.5		37.5	38.4	39.5	40.6	41.6	43.1	44.2	
97.5	99.3	100.8	103.4	106.5	108.5	110.4	Height	95.2	97.6	100.3	103.2	105.8	109.6	112.3	
22.0	22.5	23.0	23.6	24.2	24.6	25.2		21.6	22.1	22.6	23.2	23.8	24.3	24.4	
56.0	57.1	58.3	60.0	61.4	62.6	64.0		54.9	56.1	57.4	58.9	60.4	61.7	62.1	
6.0	6.2	6.4	6.7	6.8	7.1	7.3	Sitting height	5.9	6.1	6.3	6.5	6.8	7.1	7.4	
15.2	15.8	16.2	16.9	17.5	18.0	18.5		15.0	15.4	15.9	16.5	17.2	17.9	18.9	
19.7	20.1	20.6	21.1	21.8	22.5	23.2		19.4	20.0	20.3	20.9	21.5	22.2	23.2	
50.1	51.1	52.2	53.7	55.5	57.2	58.9	Head circ.	49.2	50.7	51.7	53.1	54.7	56.5	59.0	

¹) Quoted by STUART, H. C., and STEVENSON, S. S., *Physical Growth and Development*, in NELSON, *Mitchell-Nelson Textbook of Pediatrics*, Philadelphia, 1950.

4½—6 Years

(Weights are in pounds and kilograms, length measurements in inches and centimetres)

Boys

Girls

94% of the values for all normal individuals								94% of the values for all normal individuals						
80% of all values								80% of all values						
50% of all values								50% of all values						
Mean								Mean						
P ₃	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₇		P ₃	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₇
							4½ Years							
31.6	33.8	35.7	38.4	41.4	43.9	47.4	Weight	30.7	32.9	35.3	38.5	42.1	46.7	50.9
14.33	15.33	16.19	17.42	18.78	19.91	21.5		13.93	14.92	16.01	17.46	19.1	21.18	23.09
39.6	40.3	40.9	42.0	43.3	44.2	45.0	Height	38.6	39.7	40.8	42.0	43.0	44.7	45.7
100.6	102.4	104.0	106.7	109.9	112.3	114.3		98.1	100.9	103.6	106.8	109.3	113.5	116.2
22.5	23.0	23.5	24.1	24.7	25.2	25.7	Sitting height	22.1	22.6	23.1	23.7	24.3	24.8	25.4
57.1	58.3	59.6	61.3	62.8	64.0	65.4		56.1	57.4	58.7	60.2	61.7	63.1	64.5
6.2	6.4	6.5	6.8	7.1	7.3	7.5	Pelvic breadth	6.1	6.3	6.5	6.7	7.0	7.3	7.6
15.7	16.2	16.6	17.3	18.0	18.5	19.1		15.5	15.9	16.4	17.0	17.7	18.5	19.4
20.0	20.4	20.8	21.4	22.1	22.8	23.4	Chest circ.	19.6	20.2	20.6	21.2	21.8	22.6	23.5
50.7	51.7	52.9	54.4	56.3	58.0	59.3		49.8	51.3	52.3	53.7	55.4	57.3	59.6
							5 Years							
34.1	36.1	38.6	41.7	45.3	48.2	51.8	Weight	32.9	35.5	38.0	41.0	44.5	48.7	52.3
15.45	16.35	17.49	18.89	20.55	21.86	23.5		14.93	16.08	17.24	18.58	20.19	22.09	23.73
40.2	41.2	42.2	43.3	44.6	45.6	46.6	Height	40.3	40.9	41.9	43.1	44.2	45.4	46.7
102.1	104.5	107.1	110.0	113.3	115.7	118.3		101.3	104.0	106.5	109.4	112.3	115.4	118.4
22.9	23.4	24.0	24.6	25.3	25.7	26.3	Sitting height	22.6	23.1	23.6	24.2	24.8	25.3	26.9
58.2	59.5	60.9	62.6	64.2	65.4	66.8		57.3	58.6	59.9	61.4	63.0	64.4	65.9
6.3	6.7	6.8	7.1	7.4	7.6	7.8	Pelvic breadth	6.3	6.6	6.7	7.0	7.3	7.5	7.8
16.1	16.9	17.4	18.1	18.7	19.3	19.7		16.0	16.7	17.1	17.8	18.5	19.2	19.8
20.2	20.5	21.0	21.5	22.3	22.9	23.8	Chest circ.	19.8	20.1	20.4	21.0	21.8	22.5	23.7
51.2	52.0	53.2	54.8	56.6	58.2	60.5		50.4	51.0	52.1	53.6	55.3	57.2	60.2
	8.3	8.5	8.9	9.3	9.7		Calf circ.		8.3	8.6	9.0	9.4	9.7	
	21.1	21.7	22.6	23.6	24.6				21.1	21.8	22.8	23.8	24.7	
							5½ Years							
	38.8	42.0	45.6	49.3	53.1		Weight		38.0	40.8	44.0	47.2	51.2	
	17.6	19.05	20.68	22.36	24.09				17.24	18.51	19.96	21.41	23.22	
	42.6	43.8	45.0	46.3	47.3		Height		42.4	43.4	44.4	45.7	46.8	
	108.3	111.2	114.4	117.5	120.1				107.8	110.2	112.8	116.1	118.9	
23.3	23.9	24.4	25.2	25.8	26.3	26.8	Sitting height	23.1	23.6	24.1	24.7	25.3	25.9	26.5
59.3	60.7	62.1	63.9	65.6	66.8	68.2		58.6	59.9	61.2	62.7	64.3	65.8	67.3
	6.8	7.1	7.4	7.6	7.9		Pelvic breadth		6.8	7.0	7.2	7.5	7.9	
	17.4	18.0	18.7	19.4	20.1				17.4	17.8	18.4	19.1	20.0	
	20.6	21.1	21.8	22.5	23.0		Chest circ.		20.0	20.5	21.1	21.8	22.6	
	52.4	53.6	55.3	57.1	58.5				50.9	52.2	53.7	55.5	57.4	
	8.4	8.7	9.1	9.5	9.9		Calf circ.		8.5	8.8	9.2	9.6	10.0	
	21.4	22.2	23.1	24.1	25.2				21.5	22.3	23.3	24.3	25.3	
							6 Years							
38.5	40.9	44.4	48.3	52.1	56.4	61.1	Weight	37.2	39.6	42.9	46.5	50.2	54.2	58.7
17.46	18.55	20.14	21.91	23.63	25.58	27.71		16.87	17.96	19.46	21.09	22.77	24.58	26.63
42.7	43.8	44.9	46.3	47.6	48.6	49.7	Height	42.5	43.5	44.6	45.6	47.0	48.1	49.4
108.5	111.2	114.1	117.5	120.8	123.5	126.2		108.0	110.6	113.2	115.9	119.3	122.3	125.4
23.8	24.3	24.9	25.7	26.3	26.8	27.4	Sitting height	23.6	24.1	24.6	25.2	25.8	26.4	27.0
60.4	61.8	63.3	65.2	66.9	68.2	69.6		59.9	61.2	62.5	64.1	65.6	67.1	68.7
	7.0	7.2	7.5	7.8	8.1		Pelvic breadth		7.0	7.2	7.4	7.7	8.1	
	17.7	18.4	19.1	19.8	20.5				17.7	18.2	18.8	19.5	20.5	
	20.9	21.4	22.1	22.8	23.4		Chest circ.		20.3	20.8	21.4	22.2	22.9	
	53.2	54.4	56.1	57.9	59.5				51.5	52.9	54.5	56.3	58.2	
	8.6	8.8	9.3	9.7	10.1		Calf circ.		8.6	8.9	9.4	9.8	10.2	
	21.8	22.6	23.6	24.6	25.7				21.9	22.7	23.8	24.8	25.8	

¹) Quoted by STUART, H. C., and STEVENSON, S. S., *Physical Growth and Development*, in NELSON, *Mitchell-Nelson Textbook of Pediatrics*, Philadelphia, 1950.

6½—8 Years

(Weights are in pounds and *kilograms*, length measurements in inches and *centimetres*)

Boys

Girls

94% of the values for all normal individuals								94% of the values for all normal individuals						
80% of all values								80% of all values						
50% of all values								50% of all values						
			Mean								Mean			
P ₃	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₇		P ₃	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₇
							6½ Years							
							Weight							
							Height							
							Sitting height							
							Pelvic breadth							
							Chest circ.							
							Calf circ.							
							7 Years							
							Weight							
							Height							
							Sitting height							
							Pelvic breadth							
							Chest circ.							
							Calf circ.							
							7½ Years							
							Weight							
							Height							
							Sitting height							
							Pelvic breadth							
							Chest circ.							
							Calf circ.							
							8 Years							
							Weight							
							Height							
							Sitting height							
							Pelvic breadth							
							Chest circ.							
							Calf circ.							
							Weight							
							Height							
							Sitting height							
							Pelvic breadth							
							Chest circ.							
							Calf circ.							

¹) Quoted by STUART, H. C., and STEVENSON, S. S., *Physical Growth and Development*, in NELSON, *Mitchell-Nelson Textbook of Pediatrics*, Philadelphia, 1950.

Boys

Girls

94% of the values for all normal individuals								94% of the values for all normal individuals								
80% of all values						80% of all values										
50% of all values					P ₉₇	50% of all values					P ₉₇					
P ₃	P ₁₀	P ₂₅	Mean	P ₇₅		P ₉₀		P ₃	P ₁₀	P ₂₅		Mean	P ₇₅	P ₉₀		
							8½ Years									
26.0 66.0	53.8	58.3	63.1	68.9	77.0	30.1	Weight	50.6	55.5	61.0	66.9	74.5	29.5			
	24.4	26.44	28.62	31.25	34.93		Height	22.95	25.17	27.67	30.35	33.79				
	49.5	50.8	52.3	53.9	55.1		Sitting height	49.0	50.1	51.4	52.9	54.1				
	125.7	129.1	132.8	137.0	140.0		Pelvic breadth	124.6	127.3	130.5	134.4	137.5				
	26.6	27.3	28.0	28.8	29.4		Chest circ.	25.8	26.3	26.8	27.5	28.1				
	67.7	69.3	71.2	73.2	74.8		Calf circ.	65.5	66.8	68.2	69.8	71.4				
	7.7	8.0	8.3	8.6	8.9											
	19.6	20.3	21.1	21.8	22.7											
	22.7	23.2	23.9	25.1	25.8											
	57.6	59.0	60.8	63.3	65.4											
26.4 67.0	9.5	9.9	10.4	10.8	11.4	30.6	Weight	49.1	52.6	57.9	63.8	70.5	79.1	89.9		
	24.1	25.1	26.3	27.4	28.9		Height	22.27	23.86	26.26	28.94	31.98	35.88	40.78		
	52.5	56.3	61.1	66.0	72.3		81.0	89.8	Sitting height	48.7	50.0	51.1	52.3	54.0	55.3	56.5
	23.81	25.54	27.71	29.94	32.8		36.74	40.73	Pelvic breadth	123.6	127.0	129.7	132.9	137.1	140.4	143.4
	48.9	50.5	51.8	53.3	55.0		56.1	57.2	Chest circ.	26.1	26.8	27.2	27.8	28.5	29.2	29.9
	124.2	128.3	131.6	135.5	139.8		142.6	145.3	Calf circ.	66.3	67.7	69.1	70.7	72.4	74.1	76.0
	7.8	8.1	8.4	8.7	9.1											
	19.9	20.6	21.4	22.2	23.0											
	23.0	23.6	24.3	25.4	26.2											
	58.4	59.9	61.8	64.4	66.7											
26.7 67.9	9.6	10.1	10.5	11.0	11.6	31.0	Weight	54.9	60.4	67.1	74.8	84.4	30.4			
	24.5	25.6	26.8	28.0	29.5		Height	24.2	25.4	26.8	28.1	29.5				
	58.7	63.7	69.0	76.0	85.5		89.8	Sitting height	50.9	52.0	53.5	55.1		56.4		
	26.63	28.89	31.3	34.47	38.78		40.73	Pelvic breadth	129.4	132.2	135.8	139.9		143.2		
	51.4	52.7	54.3	55.9	57.1		57.2	Chest circ.	26.4	27.0	27.6	28.2		28.9	29.6	
	130.6	134.0	137.9	142.1	145.1		145.3	Calf circ.	67.1	68.5	70.0	71.7		73.4	75.2	
	8.0	8.3	8.5	8.9	9.2											
	20.2	21.0	21.7	22.6	23.5											
	23.4	24.0	24.8	25.8	26.8											
	59.3	60.9	62.9	65.5	68.1											
27.1 68.8	9.8	10.2	10.8	11.2	11.9	31.5	Weight	53.2	57.1	62.8	70.3	79.1	89.7	101.9		
	24.9	26.0	27.3	28.5	30.1		81.0	89.8	Height	24.13	25.9	28.49	31.89	35.88	40.69	46.22
	56.8	61.1	66.3	71.9	79.6		89.9	100.0	Sitting height	50.3	51.8	53.0	54.6	56.1	57.5	58.8
	25.76	27.71	30.07	32.61	36.11		40.78	45.36	Pelvic breadth	127.7	131.7	134.6	138.6	142.6	146.0	149.3
	50.7	52.3	53.7	55.2	56.8		58.1	59.2	Chest circ.	26.7	27.3	28.0	28.7	29.3	30.0	30.6
	128.7	132.8	136.3	140.3	144.4		147.5	150.3	Calf circ.	67.8	69.4	71.1	72.8	74.5	76.3	78.3
	8.0	8.4	8.7	9.0	9.4											
	20.4	21.3	22.0	22.9	23.9											
	23.6	24.3	25.2	26.2	27.3											
	60.1	61.8	63.9	66.6	69.4											
	10.0	10.4	10.9	11.4	12.1	30.7	Weight	53.2	57.1	62.8	70.3	79.1	89.7	101.9		
	25.3	26.4	27.7	29.0	30.7		81.0	89.8	Height	24.13	25.9	28.49	31.89	35.88	40.69	46.22
	56.8	61.1	66.3	71.9	79.6		89.9	100.0	Sitting height	50.3	51.8	53.0	54.6	56.1	57.5	58.8
	25.76	27.71	30.07	32.61	36.11		40.78	45.36	Pelvic breadth	127.7	131.7	134.6	138.6	142.6	146.0	149.3

¹) Quoted by STUART, H. C., and STEVENSON, S. S., *Physical Growth and Development*, in NELSON, *Mitchell-Nelson Textbook of Pediatrics*, Philadelphia, 1950.

10½-12 Years

(Weights are in pounds and kilograms, length measurements in inches and centimetres)

Boys

Girls

94% of the values for all normal individuals								94% of the values for all normal individuals						
80% of all values						P ₉₇		80% of all values						P ₉₇
50% of all values					P ₉₀			50% of all values					P ₉₀	
P ₃	P ₁₀	P ₂₅	Mean	P ₇₅				P ₂₅	P ₅₀	P ₇₅	P ₉₀			
10½ Years							P ₃	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₇	
	63.7	69.0	74.8	83.4	94.6			59.9	66.4	74.6	84.1	95.1		
	28.89	31.3	33.93	37.83	42.91		Weight	27.17	30.12	33.79	38.15	43.14		
	53.2	54.5	56.0	57.8	58.9			52.9	54.1	55.8	57.4	58.9		
	135.1	138.4	142.3	146.8	149.7		Height	134.4	137.5	141.7	145.9	149.7		
27.4	27.9	28.6	29.4	30.3	31.0	31.8	Sitting height	27.0	27.7	28.4	29.1	29.8	30.5	31.3
69.6	71.0	72.7	74.6	76.9	78.9	80.8		68.6	70.4	72.2	73.9	75.7	77.6	79.6
	8.2	8.5	8.8	9.1	9.6		Pelvic breadth		8.3	8.5	9.0	9.4	10.0	
	20.8	21.6	22.3	23.2	24.4			21.0	21.7	22.9	24.0	25.3		
	24.0	24.7	25.5	26.6	27.8		Chest circ.		22.7	23.6	24.7	25.9	27.2	
	60.9	62.8	64.9	67.7	70.7			57.8	59.9	62.8	65.8	69.0		
	10.1	10.5	11.1	11.6	12.4		Calf circ.		10.1	10.5	11.1	11.8	12.5	
	25.7	26.8	28.1	29.5	31.4			25.6	26.8	28.3	29.9	31.8		
11 Years														
61.8	66.3	71.6	77.6	87.2	99.3	111.7	Weight	57.9	62.6	69.9	78.8	89.1	100.4	112.9
28.03	30.07	32.48	35.2	39.55	45.04	50.67		26.26	28.4	31.71	35.74	40.42	45.54	51.21
52.5	54.0	55.3	56.8	58.7	59.8	60.8	Height	52.1	53.9	55.2	57.0	58.7	60.4	62.0
133.4	137.3	140.5	144.2	149.2	151.8	154.4		132.3	137.0	140.3	144.7	149.2	153.4	157.4
27.6	28.2	28.9	29.6	30.5	31.4	32.2	Sitting height	27.4	28.1	28.9	29.6	30.4	31.2	32.0
70.2	71.7	73.4	75.3	77.6	79.8	81.7		69.6	71.5	73.4	75.3	77.2	79.2	81.2
	8.3	8.6	8.9	9.2	9.8		Pelvic breadth		8.4	8.7	9.2	9.7	10.2	
	21.1	21.8	22.6	23.5	24.8			21.4	22.2	23.5	24.6	26.0		
	24.3	25.1	26.0	27.1	28.3		Chest circ.		23.1	24.0	25.3	26.5	27.8	
	61.7	63.7	65.9	68.8	71.9			58.6	61.1	64.2	67.2	70.5		
	10.2	10.7	11.2	11.8	12.6		Calf circ.		10.2	10.7	11.4	12.0	12.8	
	26.0	27.1	28.5	30.0	32.0			26.0	27.3	28.9	30.6	32.6		
11½ Years														
	69.2	74.6	81.0	91.6	104.5		Weight		66.1	74.0	83.2	94.0	106.0	
	31.39	33.84	36.74	41.55	47.4			29.98	33.57	37.74	42.64	48.08		
	55.0	56.3	57.8	59.6	60.9		Height		55.0	56.3	58.3	60.2	61.8	
	139.8	142.9	146.9	151.4	154.8			139.8	143.1	148.1	152.9	157.0		
27.9	28.5	29.2	30.0	30.9	31.8	32.6	Sitting height	27.9	28.7	29.4	30.2	31.0	31.9	32.7
70.9	72.5	74.2	76.2	78.5	80.7	82.8		70.7	72.8	74.8	76.8	78.9	81.0	83.2
	8.5	8.7	9.1	9.4	10.0		Pelvic breadth		8.6	9.0	9.5	10.0	10.6	
	21.5	22.2	23.1	24.0	25.3			21.9	22.8	24.2	25.4	26.8		
	24.6	25.4	26.3	27.5	28.8		Chest circ.		23.4	24.6	25.8	27.0	28.4	
	62.5	64.6	66.9	69.9	73.1			59.6	62.5	65.5	68.5	72.2		
	10.4	10.9	11.4	12.0	12.9		Calf circ.		10.5	11.0	11.6	12.3	13.1	
	26.4	27.6	29.0	30.6	32.8			26.6	27.9	29.5	31.2	33.2		
12 Years														
67.2	72.0	77.5	84.4	96.0	109.6	124.2	Weight	63.6	69.5	78.0	87.6	98.8	111.5	127.7
30.48	32.66	35.15	38.28	43.55	49.71	56.34		28.85	31.52	35.38	39.74	44.82	50.58	57.92
54.4	56.1	57.2	58.9	60.4	62.2	63.7	Height	54.3	56.1	57.4	59.8	61.6	63.2	64.8
138.1	142.4	145.2	149.6	153.5	157.9	161.9		137.8	142.6	145.9	151.9	156.6	160.6	164.6
28.2	28.9	29.5	30.4	31.3	32.2	33.1	Sitting height	28.3	29.2	30.0	31.0	31.8	32.6	33.5
71.6	73.3	75.0	77.2	79.6	81.9	84.2		72.0	74.2	76.4	78.7	80.8	82.9	85.1
	8.6	8.9	9.2	9.6	10.2		Pelvic breadth		8.8	9.2	9.8	10.3	10.9	
	21.9	22.6	23.5	24.5	25.8			22.4	23.4	24.9	26.2	27.6		
	24.9	25.9	26.7	27.9	29.2		Chest circ.		23.8	25.1	26.2	27.4	29.0	
	63.3	65.5	67.8	70.9	74.2			60.6	63.8	66.7	69.7	73.8		
	10.5	11.0	11.6	12.3	13.2		Calf circ.		10.7	11.2	11.8	12.5	13.3	
	26.8	28.0	29.5	31.2	33.5			27.1	28.5	30.1	31.8	33.8		

¹) Quoted by STUART, H. C., and STEVENSON, S. S., *Physical Growth and Development*, in NELSON, *Mitchell-Nelson Textbook of Pediatrics*, Philadelphia, 1950.

Normal Body Measurements during Growth¹ (continued)
12½-14 Years

(Weights are in pounds and kilograms, length measurements in inches and centimetres)

Boys

Girls

94% of the values for all normal individuals								94% of the values for all normal individuals						
80% of all values								80% of all values						
50% of all values								50% of all values						
Mean								Mean						
P ₃	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₇		P ₃	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₇
12½ Years								12½ Years						
	74.6	80.6	88.7	102.0	116.4		Weight	74.7	83.7	93.4	104.9	118.0		
	33.84	36.56	40.23	46.27	52.8			33.88	37.97	42.37	47.58	53.52		
	56.9	58.1	60.0	61.9	63.6		Height	57.4	58.8	60.7	62.6	64.0		
	144.5	147.5	152.3	157.2	161.6			145.9	149.3	154.3	159.1	162.7		
28.5	29.2	29.9	30.8	31.9	32.8	33.8	Sitting height	29.0	29.9	30.8	31.6	32.4	33.3	34.2
72.4	74.1	76.0	78.3	81.0	83.4	86.0		73.7	76.0	78.2	80.3	82.4	84.6	86.8
	8.8	9.1	9.5	9.8	10.4		Pelvic breadth	9.1	9.4	10.0	10.5	11.1		
	22.3	23.1	24.1	25.1	26.5			23.0	24.0	25.5	26.8	28.3		
	25.2	25.8	27.2	28.5	29.8		Chest circ.	24.3	25.6	26.6	27.9	29.6		
	64.2	66.5	69.1	72.4	75.8			61.8	64.9	67.7	70.9	75.3		
	10.7	11.3	11.8	12.6	13.5		Calf circ.	10.9	11.5	12.1	12.7	13.5		
	27.3	28.6	30.1	32.0	34.2			27.7	29.1	30.7	32.4	34.3		
13 Years								13 Years						
72.0	77.1	83.7	93.0	107.9	123.2	138.0	Weight	72.2	79.9	89.4	99.1	111.0	124.5	142.3
32.66	34.97	37.97	42.18	48.94	55.88	62.6		32.75	36.24	40.55	44.95	50.35	56.47	64.55
56.0	57.7	58.9	61.0	63.3	65.1	66.7	Height	56.6	58.7	60.1	61.8	63.6	64.9	66.3
142.2	146.6	149.7	155.0	160.8	165.3	169.5		143.7	149.1	152.6	157.1	161.5	164.8	168.4
28.9	29.5	30.3	31.3	32.5	33.6	34.7	Sitting height	29.6	30.5	31.4	32.2	33.0	33.8	34.7
73.3	75.0	77.0	79.6	82.5	85.4	88.1		75.2	77.5	79.7	81.8	83.8	86.0	88.2
	8.9	9.3	9.7	10.1	10.7		Pelvic breadth	9.3	9.7	10.2	10.8	11.4		
	22.7	23.6	24.6	25.6	27.2			23.6	24.6	26.0	27.4	29.0		
	25.6	26.5	27.7	29.0	30.5		Chest circ.	24.8	25.9	27.0	28.3	30.2		
	65.0	67.4	70.3	73.8	77.4			62.9	65.9	68.6	72.0	76.7		
	10.9	11.5	12.1	12.9	13.7		Calf circ.	11.1	11.7	12.3	12.9	13.7		
	27.8	29.2	30.8	32.7	34.8			28.2	29.7	31.2	32.9	34.8		
13½ Years								13½ Years						
	82.2	89.6	100.3	115.5	130.1		Weight	85.5	94.6	103.7	115.4	128.9		
	37.29	40.64	45.5	52.39	59.01			38.78	42.91	47.04	52.35	58.47		
	58.8	60.3	62.6	64.8	66.5		Height	59.5	60.8	62.4	64.0	65.3		
	149.4	153.1	158.9	164.6	168.9			151.1	154.4	158.4	162.6	165.9		
29.2	30.0	30.9	32.0	33.2	34.4	35.4	Sitting height	30.2	31.1	31.9	32.7	33.5	34.3	35.1
74.3	76.1	78.4	81.2	84.3	87.4	89.9		76.6	78.9	81.0	83.1	85.0	87.0	89.1
	9.1	9.5	9.9	10.4	10.9		Pelvic breadth	9.5	9.9	10.4	10.9	11.6		
	23.2	24.1	25.2	26.4	27.8			24.2	25.2	26.5	27.8	29.5		
	26.1	27.1	28.5	29.9	31.3		Chest circ.	25.1	26.2	27.3	28.7	30.6		
	66.3	68.8	72.4	75.8	79.4			63.8	66.6	69.3	72.9	77.7		
	11.2	11.8	12.4	13.2	13.9		Calf circ.	11.3	11.9	12.4	13.2	13.8		
	28.5	29.9	31.6	33.4	35.3			28.7	30.2	31.6	33.4	35.1		
14 Years								14 Years						
79.8	87.2	95.5	107.6	123.1	136.9	150.6	Weight	83.1	91.0	99.8	108.4	119.7	133.3	150.8
36.2	39.55	43.32	48.81	55.84	62.1	68.31		37.69	41.28	45.27	49.17	54.29	60.46	68.4
57.6	59.9	61.6	64.0	66.3	67.9	69.7	Height	58.3	60.2	61.5	62.8	64.4	65.7	67.2
146.4	152.1	156.5	162.7	168.4	172.4	177.1		148.2	153.0	156.1	159.6	163.7	167.0	170.7
29.8	30.5	31.5	32.6	33.9	35.2	36.0	Sitting height	30.7	31.5	32.3	33.1	33.8	34.6	35.4
75.6	77.4	80.0	82.9	86.1	89.3	91.4		77.9	80.0	81.9	84.0	85.9	87.8	89.8
	9.3	9.7	10.2	10.7	11.1		Pelvic breadth	9.8	10.2	10.6	11.1	11.8		
	23.6	24.6	25.8	27.1	28.3			24.8	25.8	26.9	28.1	29.9		
	26.6	27.6	29.3	30.6	32.0		Chest circ.	25.4	26.4	27.6	29.0	31.0		
	67.6	70.2	74.5	77.8	81.4			64.6	67.2	69.9	73.7	78.6		
	11.5	12.0	12.7	13.4	14.1		Calf circ.	11.5	12.0	12.6	13.3	13.9		
	29.1	30.6	32.3	34.1	35.8			29.2	30.6	32.0	33.8	35.4		

¹) Quoted by STUART, H. C., and STEVENSON, S. S., *Physical Growth and Development*, in NELSON, *Mitchell-Nelson Textbook of Pediatrics*, Philadelphia, 1950.

14½-16 Years

(Weights are in pounds and kilograms, length measurements in inches and centimetres)

Boys

Girls

94% of the values for all normal individuals								94% of the values for all normal individuals									
80% of all values								80% of all values									
50% of all values								50% of all values									
Mean								Mean									
P ₃	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₇		P ₃	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₇			
							14½ Years										
30.3 77.0	93.3 42.32	101.9 46.22	113.9 51.66	129.1 58.56	142.4 64.59	36.5 92.7	Weight	94.2 42.73	102.5 46.49	111.0 50.35	121.8 55.25	135.7 61.55	35.5 90.2				
	61.0 155.0	62.7 159.4	65.1 165.3	67.2 170.7	68.7 174.6		Height	60.7 154.1	61.8 156.9	63.1 160.4	64.7 164.3	66.0 167.6					
	31.1 78.9	32.2 81.7	33.3 84.7	34.6 87.7	35.7 90.7		Sitting height	31.2 79.1	31.9 80.9	32.6 82.7	33.4 84.7	34.1 86.6		34.8 88.4			
	9.5 24.1	9.9 25.1	10.4 26.3	10.8 27.5	11.3 28.7		Pelvic breadth	9.9 25.2	10.3 26.2	10.7 27.2	11.2 28.4	11.9 30.3					
	27.3 69.4	28.5 72.3	30.0 76.3	31.4 79.6	32.7 83.1		Chest circ.	25.6 65.1	26.7 67.7	27.7 70.4	29.2 74.2	31.2 79.2					
	11.7 29.8	12.3 31.3	13.0 32.9	13.6 34.6	14.3 36.2		Calf circ.	11.7 29.6	12.2 30.9	12.7 32.3	13.4 34.1	14.1 35.7					
								15 Years									
	91.3 41.41	99.4 45.09	108.2 49.08	120.1 54.48	135.0 61.23		147.8 67.04	161.6 73.3	Weight	89.0 40.37	97.4 44.18	105.1 47.67		113.5 51.48	123.9 56.2	138.1 62.64	155.2 70.4
	59.7 151.7	62.1 157.8	63.9 162.3	66.1 167.8	68.1 173.0		69.6 176.7	71.6 181.8	Height	59.1 150.2	61.1 155.2	62.1 157.7		63.4 161.1	64.9 164.9	66.2 168.1	67.6 171.6
	30.9 78.5	31.7 80.6	32.8 83.4	34.0 86.3	35.1 89.2		36.2 91.9	36.9 93.7	Sitting height	31.5 80.0	32.2 81.7	32.8 83.4		33.5 85.2	34.2 87.0	34.9 88.7	35.6 90.4
	9.7 24.6	10.1 25.6	10.5 26.7	10.9 27.9	11.5 29.1		37.2 94.6	Pelvic breadth	10.1 25.6	10.4 26.5	10.8 27.5	11.3 28.7		12.1 30.6	35.6 90.5		
28.0 71.1	29.3 74.4	30.7 78.0	32.0 81.3	33.4 84.8	Chest circ.	25.8 65.5		26.8 68.1	27.9 70.9	29.4 74.7	31.4 79.8						
12.0 30.4	12.6 31.9	13.2 33.4	13.8 35.1	14.4 36.6	Calf circ.	11.8 29.9		12.2 31.1	12.8 32.6	13.5 34.3	14.1 35.9						
								15½ Years									
105.2 47.72	113.5 51.48	124.9 56.65	139.7 63.37	152.6 69.22	Weight	99.2 45.0		106.8 48.44	115.3 52.3	125.6 56.97	139.6 63.32						
63.1 160.3	64.8 164.7	66.8 169.7	68.8 174.8	70.2 178.2	Height	61.3 155.7		62.3 158.2	63.7 161.7	65.1 165.3	66.4 168.6						
31.6 80.3	32.5 82.5	33.5 85.0	34.5 87.7	35.6 90.4	36.5 92.8	37.2 94.6		Sitting height	31.8 80.7	32.4 82.3	33.0 83.9	33.7 85.6	34.4 87.4	35.1 89.0	35.6 90.5		
9.9 25.1	10.2 26.0	10.7 27.1	11.1 28.2	11.6 29.4	Pelvic breadth	10.2 25.9		10.5 26.7	10.9 27.8	11.4 29.0	12.1 30.8						
28.7 72.8	29.9 75.8	31.2 79.4	32.6 82.9	34.0 86.3	Chest circ.	25.9 65.8		26.9 68.4	28.1 71.3	29.6 75.1	31.6 80.2						
12.2 30.9	12.7 32.3	13.3 33.8	14.0 35.5	14.6 37.0	Calf circ.	11.8 30.1		12.4 31.4	12.9 32.9	13.6 34.5	14.2 36.1						
								16 Years									
103.4 46.9	111.0 50.35	118.7 53.84	129.7 58.83	144.4 65.5	157.3 71.35	170.5 77.34	Weight	91.8 41.64	100.9 45.77	108.4 49.17	117.0 53.07	127.2 57.7	141.1 64.0	157.7 71.53			
61.6 156.5	64.1 162.8	65.8 167.1	67.8 171.6	69.5 176.6	70.7 179.7	73.1 185.6	Height	59.4 150.8	61.5 156.1	62.4 158.6	63.9 162.2	65.2 165.7	66.5 169.0	67.7 172.0			
32.3 82.0	33.1 84.1	34.0 86.4	35.0 88.9	36.0 91.4	36.9 93.6	37.5 95.3	Sitting height	32.0 81.2	32.6 82.7	33.1 84.2	33.8 85.9	34.5 87.6	35.1 89.1	35.7 90.6			
10.1 25.6	10.4 26.4	10.8 27.4	11.2 28.4	11.6 29.6	11.6 29.6	11.6 29.6	Pelvic breadth	10.3 26.1	10.6 26.9	11.0 28.0	11.5 29.2	12.2 31.0	12.2 31.0				
29.3 74.4	30.4 77.2	31.8 80.7	33.3 84.5	34.6 87.8			Chest circ.	26.0 66.1	27.0 68.7	28.2 71.6	29.7 75.4	31.7 80.5					
12.3 31.3	12.8 32.7	13.5 34.2	14.1 35.8	14.7 37.3			Calf circ.	11.9 30.3	12.4 31.6	13.0 33.1	13.7 34.6	14.3 36.3					

¹) Quoted by STUART, H. C., and STEVENSON, S. S., *Physical Growth and Development*, in NELSON, *Mitchell-Nelson Textbook of Pediatrics*, Philadelphia, 1950.

Boys								Girls							
94% of the values for all normal individuals								94% of the values for all normal individuals							
80% of all values								80% of all values							
50% of all values								50% of all values							
			Mean								Mean				
P ₃	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₇		P ₃	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₇	
							16½ Years								
	114.3	121.6	133.0	147.9	161.0		Weight	101.9	109.4	118.1	128.4	142.2			
	51.85	55.16	60.33	67.09	73.03			46.22	49.62	53.57	58.24	64.5			
	64.6	66.3	68.0	69.8	71.1		Height	61.5	62.5	63.9	65.3	66.6			
	164.2	168.4	172.7	177.4	180.7			156.2	158.8	162.4	165.9	169.2			
32.8	33.6	34.4	35.4	36.3	37.1	37.8	Sitting height	32.1	32.7	33.2	33.9	34.5	35.1	35.7	
83.2	85.2	87.5	89.8	92.1	94.2	95.9		81.4	82.9	84.4	86.1	87.7	89.2	90.7	
	10.2	10.5	10.9	11.3	11.7		Pelvic breadth		10.3	10.6	11.1	11.5	12.2		
	25.9	26.7	27.6	28.6	29.8				26.2	27.0	28.2	29.3	31.1		
	29.7	30.8	32.1	33.6	35.0		Chest circ.		26.1	27.2	28.3	29.8	31.8		
	75.4	78.1	81.6	85.4	88.8				66.3	69.0	71.9	75.7	80.7		
	12.4	13.0	13.5	14.2	14.8		Calf circ.		12.0	12.5	13.1	13.7	14.4		
	31.5	32.9	34.4	36.1	37.6				30.5	31.8	33.3	34.8	36.5		
							17 Years								
							Weight	93.9	102.8	110.4	119.1	129.6	143.3	159.5	
110.5	117.5	124.5	136.2	151.4	164.6	175.6		42.59	46.63	50.08	54.02	58.79	65.0	72.35	
50.12	53.3	56.47	61.78	68.67	74.66	79.65	Height	59.4	61.5	62.6	64.0	65.4	66.7	67.8	
62.6	65.2	66.8	68.4	70.1	71.5	73.5		151.0	156.3	159.0	162.5	166.1	169.4	172.2	
159.0	165.5	169.7	173.7	178.1	181.6	186.6	Sitting height	32.1	32.7	33.3	33.9	34.6	35.2	35.8	
33.0	33.8	34.8	35.6	36.5	37.2	38.0		81.6	83.1	84.6	86.2	87.8	89.3	90.8	
83.9	86.0	88.4	90.4	92.7	94.6	96.4	Pelvic breadth		10.4	10.7	11.1	11.6	12.3		
	10.3	10.6	10.9	11.3	11.8				26.3	27.1	28.3	29.4	31.2		
	26.1	26.9	27.8	28.7	29.9		Chest circ.		26.2	27.3	28.4	29.9	31.8		
	30.1	31.1	32.5	33.9	35.3				66.4	69.2	72.1	75.9	80.9		
	76.4	78.9	82.5	86.2	89.7		Calf circ.		12.0	12.6	13.1	13.7	14.4		
	12.5	13.0	13.6	14.3	14.9				30.6	31.9	33.4	34.9	36.6		
	31.7	33.1	34.6	36.3	37.8		17½ Years								
							Weight		103.2	110.8	119.5	130.2	143.9		
	118.8	125.8	137.6	153.6	166.8				46.81	50.26	54.2	59.06	65.27		
	53.89	57.06	62.41	69.67	75.66		Height		61.5	62.6	64.0	65.4	66.7		
	65.3	67.0	68.5	70.3	71.6				156.3	159.0	162.5	166.1	169.4		
	165.9	170.1	174.1	178.5	182.0		Sitting height	32.1	32.7	33.3	34.0	34.6	35.2	35.8	
33.2	34.0	35.0	35.7	36.6	37.4	38.1		81.7	83.2	84.7	86.3	87.9	89.4	90.8	
84.4	86.5	88.8	90.7	93.1	94.9	96.7	Pelvic breadth		10.4	10.7	11.2	11.6	12.3		
	10.3	10.6	11.0	11.3	11.8				26.4	27.2	28.4	29.5	31.3		
	26.3	27.0	27.9	28.8	30.0		Chest circ.		26.2	27.3	28.4	29.9	31.9		
	30.3	31.2	32.7	34.1	35.5				66.5	69.3	72.2	76.0	81.0		
	77.0	79.4	83.0	86.7	90.2		Calf circ.		12.1	12.6	13.2	13.8	14.4		
	12.5	13.1	13.7	14.4	15.0				30.7	32.0	33.5	35.0	36.7		
	31.8	33.3	34.8	36.5	38.0		18 Years								
							Weight	94.5	103.5	111.2	119.9	130.8	144.5	160.7	
113.0	120.0	127.1	139.0	155.7	169.0	179.0		42.87	46.95	50.44	54.39	59.33	65.54	72.89	
51.26	54.43	57.65	63.05	70.62	76.66	81.19	Height	59.4	61.5	62.6	64.0	65.4	66.7	67.8	
62.8	65.5	67.0	68.7	70.4	71.8	73.9		151.0	156.3	159.0	162.5	166.1	169.4	172.2	
159.6	166.3	170.5	174.5	178.9	182.4	187.6	Sitting height	32.1	32.7	33.3	34.0	34.6	35.2	35.8	
33.3	34.2	35.0	35.8	36.7	37.4	38.1		81.7	83.2	84.7	86.3	87.9	89.4	90.8	
84.7	86.8	89.0	90.9	93.4	95.0	96.8	Pelvic breadth		10.4	10.7	11.2	11.6	12.3		
	10.4	10.7	11.0	11.4	11.8				26.4	27.2	28.4	29.5	31.3		
	26.5	27.1	28.0	28.9	30.1		Chest circ.		26.2	27.3	28.5	30.0	31.9		
	30.5	31.4	32.8	34.3	35.7				66.6	69.4	72.3	76.1	81.1		
	77.5	79.8	83.4	87.1	90.7		Calf circ.		12.1	12.6	13.2	13.8	14.5		
	12.6	13.2	13.7	14.4	15.0				30.8	32.1	33.6	35.1	36.8		
	31.9	33.4	34.9	36.6	38.1										

¹) Quoted by STUART, H. C., and STEVENSON, S. S., *Physical Growth and Development*, in NELSON, *Mitchell-Nelson Textbook of Pediatrics*, Philadelphia, 1950.

Body length of the embryo
(Rule of AHLFELD and HAASE)

Months of 28 days	1st month	1 × 1	1 cm	crown to heel length, body extended
	2nd month	2 × 2	4 cm	
	3rd month	3 × 3	9 cm	
	4th month	4 × 4	16 cm	
	5th month	5 × 5	25 cm	
	6th month	6 × 5	30 cm	
	7th month	7 × 5	35 cm	
	8th month	8 × 5	40 cm	
	9th month	9 × 5	45 cm	
	10th month	10 × 5	50 cm	

Diameter of the chorion, crown-heel and crown-rump lengths, and weight of the embryo¹

Age of the embryo	Crown-rump length mm	Crown-heel length mm	External diameter of the chorion mm	Weight grams
1 week	0.1 ²	—	0.2	—
2 weeks	0.2 ²	—	3	—
3 weeks	2.0	—	10	—
4 weeks	5.0	—	20	0.02
5 weeks	8.0	—	25	—
6 weeks	12.0	—	30	—
7 weeks	17.0	19.0	40	—
8 weeks	23.0	30.0	50	1
12 weeks	56.0	73.0	—	14
16 weeks	112.0	157.0	—	105
20 weeks	160.0	239.0	—	310
24 weeks	203.0	296.0	—	640
28 weeks	242.0	355.0	—	1080
32 weeks	277.0	409.0	—	1670
36 weeks	313.0	458.0	—	2400
Full term (266 days)	350.0	500.0	—	3300

Weight changes during the first
days of life
(after GREGORY)

Gain in weight of the infant³

Hours	Days	Loss ounces (<i>grams</i>)			Breast-fed children						Artificially-fed boys and girls		
					boys			girls					
					lb.	oz.	(<i>kg</i>)	lb.	oz.	(<i>kg</i>)	lb.	oz.	(<i>kg</i>)
0- 12	1st	2.8 (<i>81</i>)	4.9 (<i>139</i>)	Weight at birth	7	11	(<i>3.48</i>)	7	2	(<i>3.24</i>)	7	8	(<i>3.39</i>)
12- 24		2.0 (<i>58</i>)		End of the 4th week	9	3	(<i>4.17</i>)	8	6	(<i>3.81</i>)	8	4	(<i>3.73</i>)
24- 36	2nd	1.8 (<i>52</i>)	2.3 (<i>64</i>)	” ” ” 8th ”	11	3	(<i>5.08</i>)	10	1	(<i>4.56</i>)	9	9	(<i>4.34</i>)
36- 48		0.4 (<i>12</i>)		” ” ” 12th ”	12	15	(<i>5.87</i>)	11	10	(<i>5.27</i>)	10	15	(<i>4.95</i>)
		Gain		” ” ” 16th ”	14	8	(<i>6.58</i>)	13	0	(<i>5.90</i>)	12	6	(<i>5.61</i>)
				” ” ” 20th ”	15	12	(<i>7.14</i>)	14	6	(<i>6.52</i>)	13	13	(<i>6.27</i>)
48- 60	3rd	0.3 (<i>8</i>)	1.2 (<i>33</i>)	” ” ” 24th ”	16	14	(<i>7.65</i>)	15	4	(<i>6.92</i>)	15	3	(<i>6.90</i>)
60- 72		0.9 (<i>25</i>)		” ” ” 28th ”	17	15	(<i>8.14</i>)	16	4	(<i>7.38</i>)	16	1	(<i>7.30</i>)
72- 84	4th	0.7 (<i>20</i>)	1.8 (<i>50</i>)	” ” ” 32nd ”	18	13	(<i>8.54</i>)	17	3	(<i>7.80</i>)	17	1	(<i>7.75</i>)
84- 96		1.1 (<i>30</i>)		” ” ” 36th ”	19	10	(<i>8.90</i>)	17	14	(<i>8.09</i>)	17	15	(<i>8.13</i>)
96-108	5th	0.9 (<i>25</i>)	1.8 (<i>50</i>)	” ” ” 40th ”	20	5	(<i>9.22</i>)	18	8	(<i>8.40</i>)	18	4	(<i>8.27</i>)
108-120		0.9 (<i>25</i>)		” ” ” 44th ”	21	4	(<i>9.65</i>)	19	3	(<i>8.72</i>)	19	1	(<i>8.65</i>)
120-132	6th	0.7 (<i>20</i>)	1.3 (<i>36</i>)	” ” ” 48th ”	22	0	(<i>9.97</i>)	19	12	(<i>8.97</i>)	19	10	(<i>8.91</i>)
132-144		0.6 (<i>16</i>)		” ” ” 52nd ”	22	9	(<i>10.21</i>)	21	5	(<i>9.66</i>)	22	0	(<i>9.98</i>)

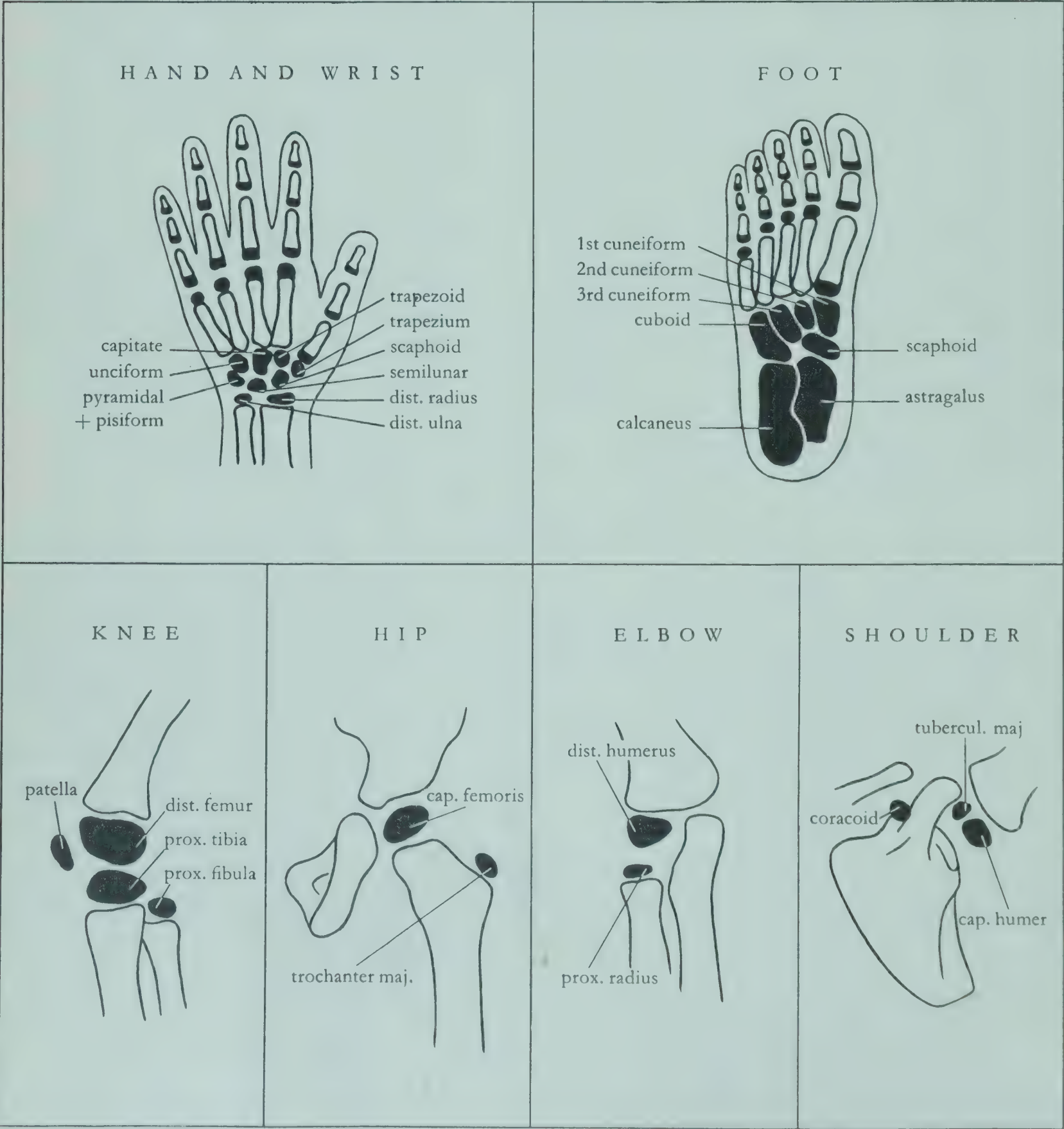
Daily gain in weight of breast-fed children

Up to the 4th week	ca.	17 drachms	(30 grams)
From the 5th - 12th "	"	15-16 "	(26-28 ")
" " 13th - 20th "	"	11-14 "	(20-24 ")
" " 21st - 36th "	"	9-10 "	(16-18 ")
" " 37th - 52nd "	"	6- 8 "	(10-15 ")

¹⁾ After AREY, L. B., *Developmental Anatomy*, Philadelphia, 1949.
²⁾ Total length of the embryonic disc.
³⁾ The ideal weight of the infant may be calculated roughly by means of the following formula: weight at birth + (a × age in months), where a = 21 oz. (600 g) during the first 6 months, and 17½ oz. (500 g) during the second 6 months (after SALMI, T., in FANCONI and WALLGREN, *Lehrbuch der Pädiatrie*, Basle, 1954).

Various methods for the assessment of skeletal development have been devised. They usually consist of the examination of one particular skeletal region, e.g. the hand or the foot (see the next page), on the assumption that its development is representative of the ossification of the whole skeleton. Such methods are not always reliable since the rates of ossification in the different regions are not always the same. CAFFEY (*Pediatric X-Ray Diagnosis*, Chicago, 1950) therefore recommends the method of SONTAG et al. (*Amer. J. Dis. Child.*, **58**, 949, 1939) for the determination of the skeletal age. The technique is as follows: X-ray photographs of the whole of the left half of the body, including the scapula, are taken, the ossification centres counted (see diagrams below), and the numbers compared with the ideal values given in the adjacent table. In counting the centres all those present in the long bones of the arms, hands, legs and feet, in the carpal and tarsal bones and in the coracoid of the scapula are included, and in older children also that of the trochanter major femoris.

Age in months	Numbers of ossification centres					
	Boys			Girls		
	Mean	Normal range ¹ (mean \pm 2 σ)	Standard deviation ¹ σ	Mean	Normal range ¹ (mean \pm 2 σ)	Standard deviation ¹ σ
1	4.11	1.29– 6.93	<i>1.41</i>	4.58	1.06– 8.10	<i>1.76</i>
3	6.63	2.91–10.35	<i>1.86</i>	7.78	3.46–12.10	<i>2.16</i>
6	9.61	5.71–13.51	<i>1.95</i>	11.44	6.26–16.62	<i>2.59</i>
9	11.88	6.56–17.20	<i>2.66</i>	15.36	5.52–25.20	<i>4.92</i>
12	13.96	6.04–21.88	<i>3.96</i>	22.40	8.54–36.26	<i>6.93</i>
18	19.27	6.04–32.48	<i>6.61</i>	34.10	17.22–50.98	<i>8.44</i>
24	29.31	13.01–35.49	<i>8.10</i>	43.44	30.14–56.74	<i>6.65</i>
30	37.59	22.79–52.39	<i>7.40</i>	48.91	35.91–61.91	<i>6.50</i>
36	43.42	32.74–54.10	<i>5.34</i>	52.73	41.77–63.69	<i>5.48</i>
42	47.06	36.66–57.46	<i>5.20</i>	56.61	48.65–64.57	<i>3.98</i>
48	51.24	42.24–60.24	<i>4.50</i>	57.94	50.12–65.76	<i>3.91</i>
54	53.94	44.24–62.64	<i>4.35</i>	59.89	53.17–66.61	<i>3.36</i>
60	56.24	48.10–64.38	<i>4.07</i>	61.52	56.14–66.90	<i>2.69</i>



¹⁾ Normal range: the limits of the normal range are strictly defined by the formula: **mean \pm 2 \times standard deviation σ** (see page 32). The normal range thus calculated is indicated in these tables by **bold figures for the mean** and *italic figures for the standard deviation*. When not so indicated the range must be regarded as purely arbitrary.

After VOGT and VICKERS, *Radiology*, 31, 441, 1938

BOYS				GIRLS			
Number of cases	P ₉₀	P ₅₀ (mean)	P ₁₀	Number of cases	P ₉₀	P ₅₀ (mean)	P ₁₀
Birth	116			Birth	112		
6 months	92			6 months	91		
1 year	101			1 year	101		
1 1/2 years	81			1 1/2 years	80		
2 years	90			2 years	86		
2 1/2 years	78			2 1/2 years	75		
3 years	78			3 years	81		
3 1/2 years	70			3 1/2 years	67		
4 years	66			4 years	61		
4 1/2 years	53			4 1/2 years	56		
5 years	52			5 years	53		
5 1/2 years	40			5 1/2 years	41		
6 years	31			6 years	32		
6 1/2 years	19			6 1/2 years	17		

80% of all normal cases

80% of all normal cases

(For the significance of the indices P₉₀, P₅₀ and P₁₀, see page 256)

After VOGT and VICKERS, *Radiology*, 31, 441, 1938



80% of all normal cases

80% of all normal cases

(For the significance of the indices P₉₀, P₅₀ and P₁₀, see page 256)

After SCHOUR and MASSLER, *J. Amer. dent. Ass.*, 28, 1153, 1941

PERMANENT TEETH

MIXED TEETH

DECIDUOUS TEETH



Foetus up to 1 1/2 years

2-6 years

7-10 years

11-35 years

Blood ¹	Ante partum			Post partum		
	10th–15th week	26th–35th week	36th week to full term	2nd–6th day	10th–15th day	
Erythrocytes (millions/mm ³)	3.61–5.29	3.12–4.64	3.45–5.05	3.05–4.69	3.00–5.25	Range*
Haematocrit (%)	33.0–46.2	28.7–45.1	30.0–46.1	28.4–43.6	26.1–48.1	„
Haemoglobin (g/100 ml)	10.2–17.0	8.9–16.1	9.8–16.2	8.5–15.7	7.9–15.9	„
Mean erythrocyte volume (μm ³)	90	94	89.9	93.8	94	Mean
Mean corpuscular haemoglobin (μg per million erythrocytes)	30.4	29.7	28.6	–	27.2	„
Mean corpuscular haemoglobin concentration (% of erythrocytes)	34.2	32.9	32.5	–	31.1	„
Electrical conductivity (as % NaCl)	0.756–0.804	0.750–0.810	0.645–0.801	0.763–0.819	0.762–0.802	Range*
Total bases (milliequivalents)	148.7–160.5	144–160.4	138.6–162.6	146.7–159.1	140.7–166.3	„
CO ₂ content of serum (vol%)	53	54	53	54	55	Mean
pH of serum	7.4	7.39	7.39	7.39	7.39	„
NaCl (serum) (mg/100 ml)	577.3–629.3	583.7–630.9	573.7–636.5	571.7–622.9	585–629.4	Range*
Plasma fibrinogen (mg/100 ml)	200–600	130–730	200–720	250–850	230–630	„
Serum protein (g/100 ml)	5.9–7.5	5.6–7.2	5.7–7.3	4.9–7.3	5.8–7.8	„
Plasma cholesterol (mg/100 ml)	112.5–426.5	180.6–334.6	137.1–525.1	157.7–463.7	102.1–512.1	„

* Range = mean ± 2 × standard deviation; see page 32 and footnote page 268.

Plasma volume and water balance²

The plasma volume increases markedly during pregnancy, reaching a maximum between the 68th and 5th day before parturition. The increase amounts to 49% of the volume 30 days after parturition. During the last weeks of pregnancy there is a significant decrease in the plasma volume amounting on the average to about 25% of the above-mentioned maximum increase. The value returns to normal by the 30th day after parturition.

During pregnancy there is an increase in the volume of the extravascular fluid, particularly in the last trimester and showing no decrease shortly before parturition. During the first week after confinement the volume decreases by 2500 ml; between the 26th and 66th day after parturition the decrease amounts to 59% of the maximum value during pregnancy.

The increases in the vascular and extravascular fluids show related changes in that during the 1st and 2nd trimesters the plasma volume increases more rapidly than the extravascular fluid, while during the 3rd trimester the reverse is the case.

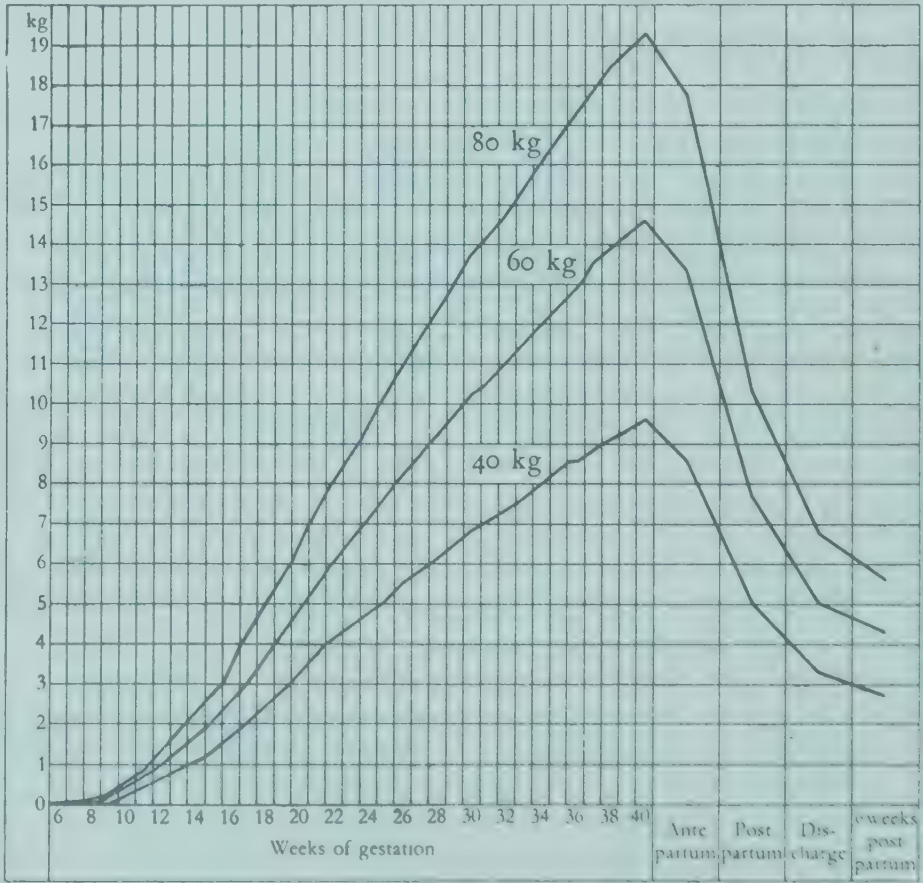
Blood constituents showing deviations from the normal during pregnancy³

	Range
Proteins	5.8–7.9 g/100 ml
Albumin	2.9–4.3 g/100 ml
Globulin	2.3–3.8 g/100 ml
Albumin/globulin ratio	1.0–1.8
Calcium	8.6–9.5 mg/100 ml
Chlorides (as NaCl)	494–612 mg/100 ml
CO ₂	45–58 vol%
Phosphatase	increase during labour
Phospholipids	195 mg/100 ml
Fatty acids	362 mg/100 ml
Neutral fats	154 mg/100 ml

Lipids During pregnancy the serum lipid concentration increases. The phospholipid level usually starts to rise during the 1st trimester, followed by an increase in the cholesterol level. The neutral fats also increase rapidly. The increase of serum lipids sometimes occurs later, occasionally as late as the 8th month.

Normal weight changes during pregnancy⁴

	%	lb. oz. (kg)
Increase in weight up to the 40th week	24.10	30 10 (13.9)
Loss of weight before parturition	1.58	2 7 (1.11)
Loss of weight during parturition	7.74	11 13 (5.35)
Loss of weight during the first 10 days post partum	3.77	5 1 (2.30)
Loss of weight during the 5 weeks post partum	1.11	1 8 (0.68)



¹) DIECKMANN and WEGNER, *Arch. intern. Med.*, **53**, 71, 188, 353, 1934. ²) MOORE et al., *Amer. J. Obstet. Gynec.*, **57**, 481, 1949. ³) STANDER and PASTORI, *Amer. J. Obstet. Gynec.*, **39**, 928, 1940 (statistical material from 2935 cases). ⁴) DIECKMANN, W. J., *Toxemias of Pregnancy*, St. Louis, 1941.

Normal weight changes during pregnancy (for weights at commencement of pregnancy of 40, 60 and 80 kg). After STANDER and PASTORE, *loc. cit.*³.

Pregnancy, Parturition and the Puerperium (continued) Plasma protein fractions before, during and after pregnancy

273

After MACK, H. C., *The Plasma Proteins in Pregnancy*, Springfield, 1955 (Values in grams per 100 millilitres plasma)

	No. of Subjects	No. of Determinations	Albumin	Globulins					Albumin/Globulin Ratio	Total Protein
				Alpha ₁	Alpha ₂	Beta	Gamma	Fibrinogen		
Non-pregnant women	12	22								
Mean			4.65	0.36	0.68	1.01	0.97	0.51	1.32	8.18
Range			3.92-5.31	0.26-0.53	0.54-0.92	0.83-1.22	0.77-1.26	0.38-0.68	1.16-1.56	6.87-9.62
Pregnant women										
First Trimester (4-7 weeks)	3	3								
Mean			4.22	0.40	0.70	0.96	0.73	0.55	1.26	7.56
Range			3.79-4.62	0.32-0.45	0.67-0.76	0.90-1.04	0.64-0.87	0.51-0.57	1.20-1.34	6.88-8.06
Second Trimester (17-26 weeks)	7	7								
Mean			3.89	0.44	0.77	1.20	0.69	0.58	1.06	7.57
Range			3.27-4.41	0.34-0.53	0.65-1.00	0.92-1.48	0.56-0.83	0.49-0.73	0.94-1.21	6.57-8.70
Third Trimester (28-41 weeks)	14	15								
Mean			3.43	0.51	0.87	1.36	0.68	0.65	0.84	7.50
Range			2.43-4.07	0.32-0.72	0.66-1.15	0.94-1.95	0.46-0.90	0.50-0.92	0.64-1.11	5.96-8.68
Delivery	16	16								
Mean			3.41	0.48	0.94	1.40	0.62	0.70	0.82	7.55
Range			2.51-4.60	0.40-0.66	0.46-1.32	1.11-1.93	0.32-0.87	0.45-1.07	0.59-0.96	5.86-10.26
Post partum										
12-24 hours	3	3								
Mean			2.68	0.54	0.86	1.22	0.50	0.67	0.71	6.47
Range			2.45-2.91	0.43-0.66	0.58-1.10	1.17-1.29	0.44-0.56	0.61-0.76	0.68-0.75	5.93-7.23
5-6 days	9	9								
Mean			3.15	0.69	1.10	1.38	0.54	0.69	0.72	7.55
Range			2.78-3.58	0.59-0.77	0.71-1.29	1.17-1.57	0.27-0.64	0.54-0.90	0.63-0.85	6.67-8.48
6-12 weeks	13	13								
Mean			4.07	0.42	0.66	1.05	0.78	0.43	1.22	7.41
Range			3.40-4.71	0.33-0.51	0.59-0.89	0.83-1.29	0.27-1.15	0.28-0.65	1.06-1.60	6.26-8.20
Maternal venous blood (delivery)	11	11								
Mean			3.46	0.49	0.97	1.41	0.64	0.73	0.82	7.71
Range			2.59-4.60	0.40-0.66	0.79-1.32	1.11-1.93	0.32-0.87	0.45-1.07	0.59-0.96	6.80-10.26
Corresponding cord blood	11	11								
Mean			3.73	0.32	0.54	0.57	0.87	0.43	1.36	6.47
Range			2.95-4.57	0.18-0.55	0.38-0.76	0.37-0.91	0.60-1.16	0.29-0.65	1.14-1.79	5.44-8.60

Remarks (for a bibliographical review see ¹⁾

In general these largely quantitative plasma protein changes^{2,3} may be seen as adaptations of the maternal organism made in response to the physiological stresses of pregnancy and designed to meet the needs of the growing foetus. The fall in the albumin level and the rise in the total globulin level start in the 1st trimester and progress until delivery. The latter is unable to compensate for the former, so that the overall picture is one of a fall in the total protein level. However, because of the increase in the total blood volume during pregnancy (see the opposite page) this does not mean that there is necessarily a deficiency of available total protein or albumin in the blood. In fact, the total amount of circulating protein in the body may even be increased compared to the pre-pregnant state.

The changing protein levels may be caused by the readier diffusion of the smaller albumin molecules into the tissues and across the placental membranes, and to failure of albumin synthesis to keep up with albumin utilization. On the whole, a state approaching protein deficiency is to be expected as a result of the enormously increased protein demand in pregnancy. Clinically, therefore, it is important that ample protein intake be maintained and debilitating states avoided as far as possible.

The plasma protein relations in cord blood correspond more nearly to these of non-pregnant women than to those of the maternal blood. The changes in the latter may thus be seen as contriving to provide the infant at birth with a normal blood pattern adequate to its needs. On the relation between foetal plasma proteins and maternal nutrition see ⁴⁻⁶.

The rise in the level of total globulins aids in compensating osmotically for

the lesser number of albumin molecules and thus in preventing fluid losses to the tissues (oedema of pregnancy). The α - and β -globulins carry most of the plasma lipids and the increase in the levels of these two fractions may therefore be related to the lipaemia and hypercholesteraemia of pregnancy.

In view of the association of the γ -globulins with antibodies the diminished concentration of this fraction is of clinical significance in pregnancy from the point of view of impairment of both acquired immunity and of the ability to form antibodies to acquired infection⁷. This is borne out by the high incidence of puerperal sepsis following undernourished pregnancies and by the susceptibility of pregnant women to the paralyzing effects of the poliomyelitis virus. The γ -globulin level in cord blood is markedly higher than in the maternal blood and it is noteworthy that intra-uterine transplacental transmission of poliomyelitis to the foetus is rare. The high foetal γ -globulin level is acquired at the expense of the maternal blood via the placenta and may be due to selective filtration of γ -globulins by the latter. It probably contributes to the relatively high resistance shown by newborn infants to the ordinary bacterial and virus infections. On the relations between immune mechanisms and plasma γ -globulin levels in the newborn see ⁸ and ⁹.

The high level of fibrinogen in the maternal plasma and the low level in cord blood are no doubt due to the poor diffusibility of these large and asymmetric molecules. The result is that the maternal organism is provided with some protection against haemorrhage whereas the newborn infant (also deficient in prothrombin¹⁰), and especially the premature one, is peculiarly susceptible to haemorrhagic diatheses. The high fibrinogen level may also account for the tendency of pregnant women to develop phlebothromboses.

¹⁾ ALHA, A.-L., *Ann. Chir. Gynaec. Fenn.*, **39**, Suppl. 4, 1950. ²⁾ CORYELL et al, *J. clin. Invest.*, **29**, 1559, 1950. ³⁾ MACY, I. G., and MACK, H. C., *Physiological Changes in Plasma Proteins Characteristic of Human Reproduction*, Detroit, 1952. ⁴⁾ DIECKMANN et al., *J. Amer. diet. Ass.*, **27**, 1046, 1951. ⁵⁾ SMITH, C. A., et al., *J. Obstet. Gynec.*, **1**, 46, 1953. ⁶⁾ TOVERUD et al., *Nat. Research Council Bull.*, **123**, 1950. ⁷⁾ CANNON, P. R., in YOUNG, J. B., *Plasma Proteins*, Springfield, 1950. ⁸⁾ SMITH, C. A., *The Physiology of the Newborn Infant*, 2nd ed., Springfield, 1951. ⁹⁾ BRAMBELL et al., *Antibodies and Embryos*, London, 1951. ¹⁰⁾ STRAUPE-JORD, J. V., and QUARF, M. L., *Proc. Soc. exp. Biol. (N. Y.)*, **61**, 369, 1946.

Plasma proteins and specific gravity of whole blood¹

	Plasma proteins (g/100 ml plasma)		Specific gravity (whole blood)	
	Minimum	Maximum	Minimum	Maximum
During the last months of pregnancy (primiparas)	5.0	7.2	1.030	1.040
During the last months of pregnancy (multiparas)	5.0	7.2	1.033	1.040
At the start of labour	5.9	6.9	1.033	1.046
During delivery	6.4	7.0	1.037	1.047
7-9 days after delivery	6.2	7.6	1.039	1.050
In the umbilical veins	5.3	6.7	1.040	1.051

Hormones during pregnancy:

Gonadotropic hormones, page 179; lactogenic hormone, page 181; oestrogens, page 201; progesterone (pregnanediol), page 202.

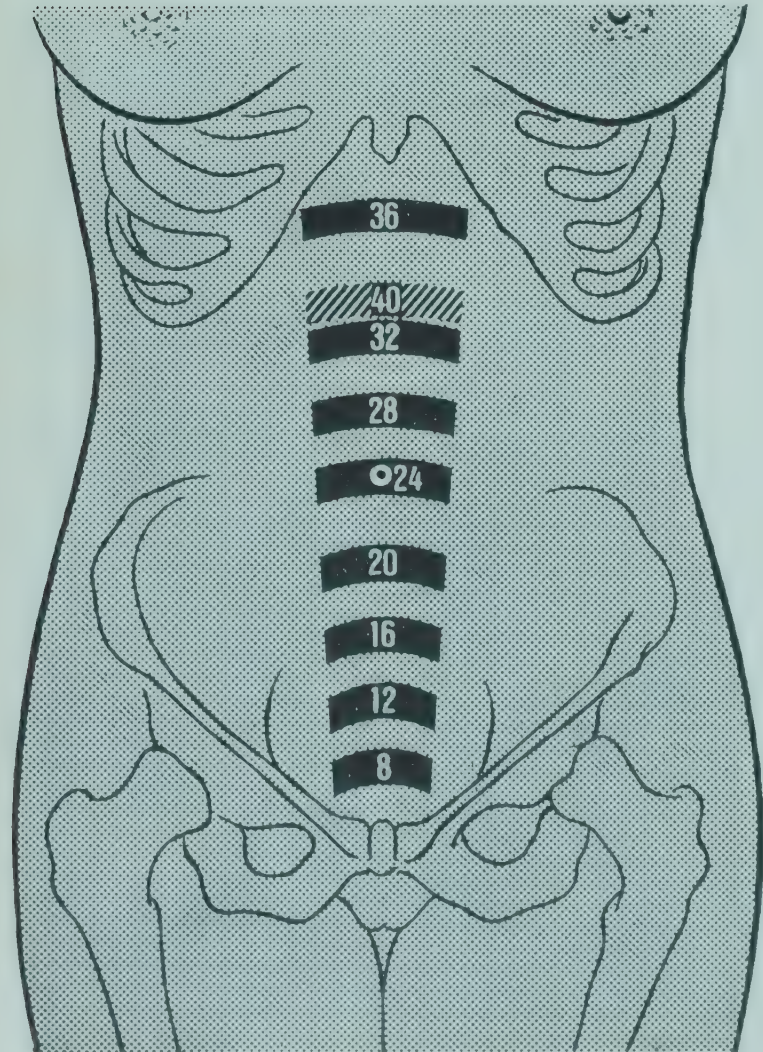
Breast milk, see pages 228, 229 and 238.

Basal metabolism during pregnancy,
see Basal Metabolism, pages 244 and 248.

Involution of the uterus after parturition²

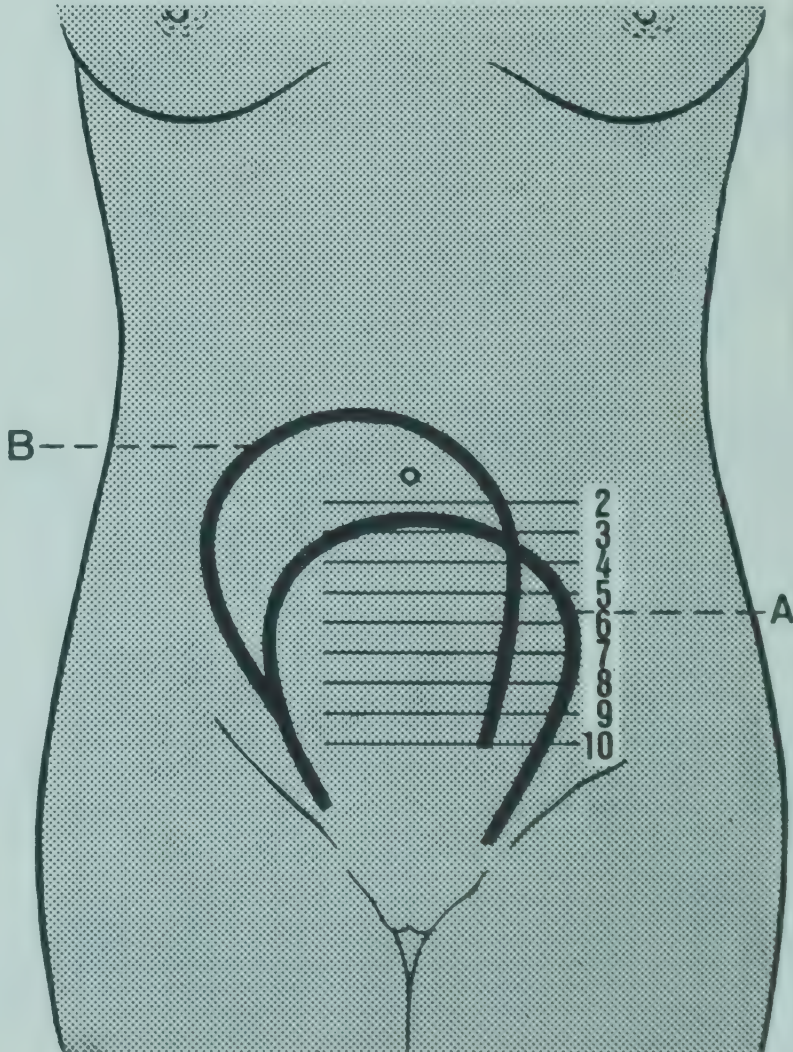
Days post partum	Height (cm)	Breadth (cm)
1	10.91	11.0
2	13.55	12.27
3	11.16	10.93
4	10.21	10.27
5	9.29	9.66
6	8.22	8.96
7	7.61	8.32
8	7.32	8.19

Development of the uterus during pregnancy



Numbers = weeks

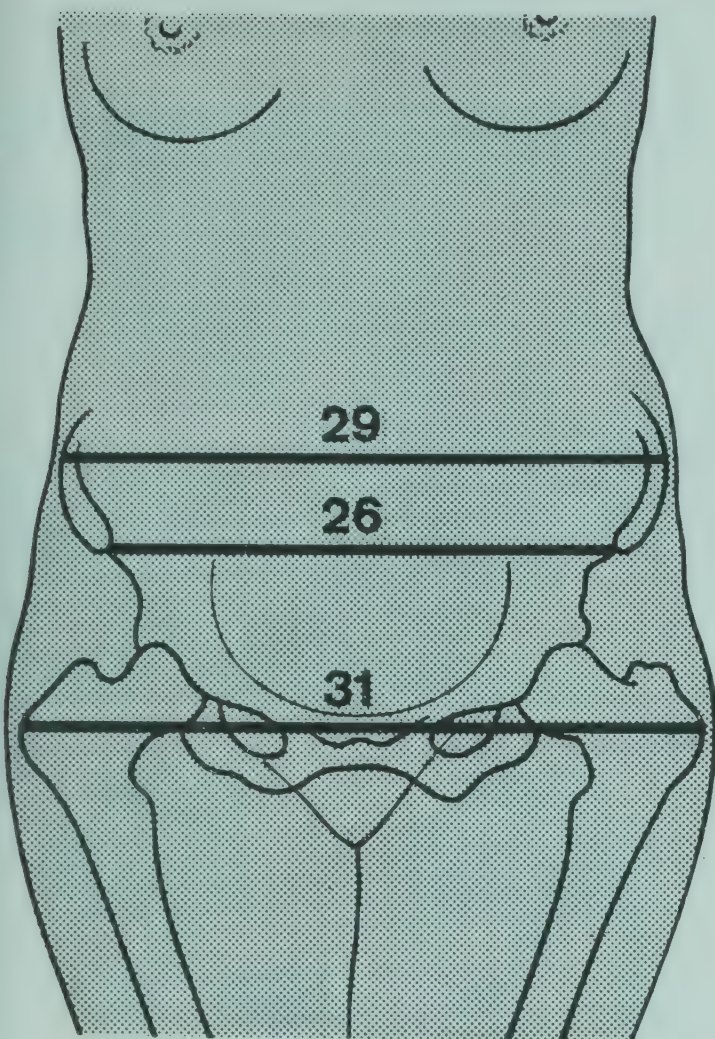
Height of the uterus post partum (bladder empty)



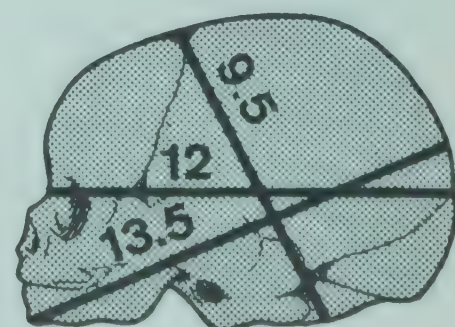
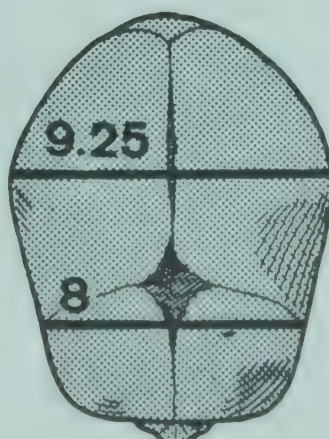
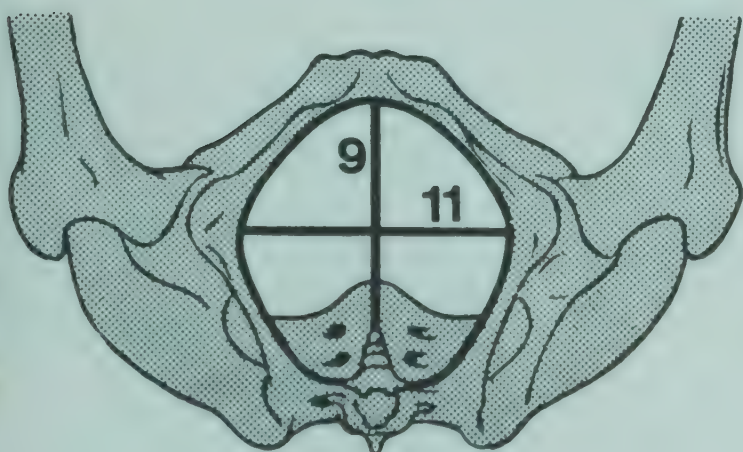
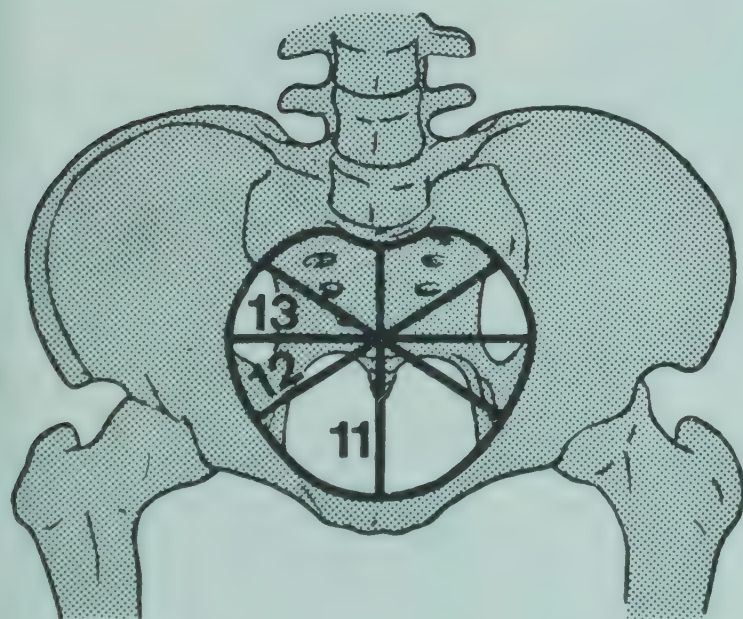
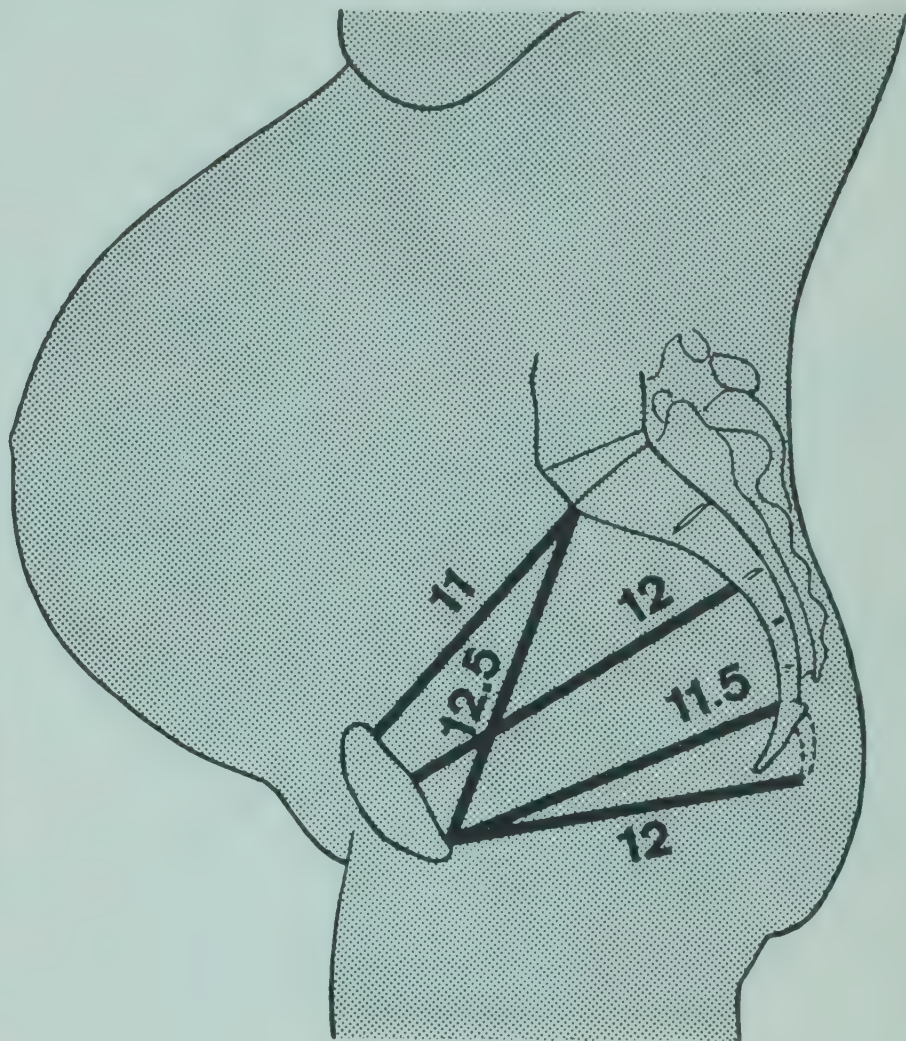
A = immediately after delivery; B = first day post partum; numbers = days post partum.

¹) After OBERST and PLASS, *Amer. J. Obstet. Gynec.*, **31**, 61, 1936.
²) After DE LEE and GREENHILL, *Principles and Practice of Obstetrics*, Philadelphia, 1947.

(measurements in centimetres)

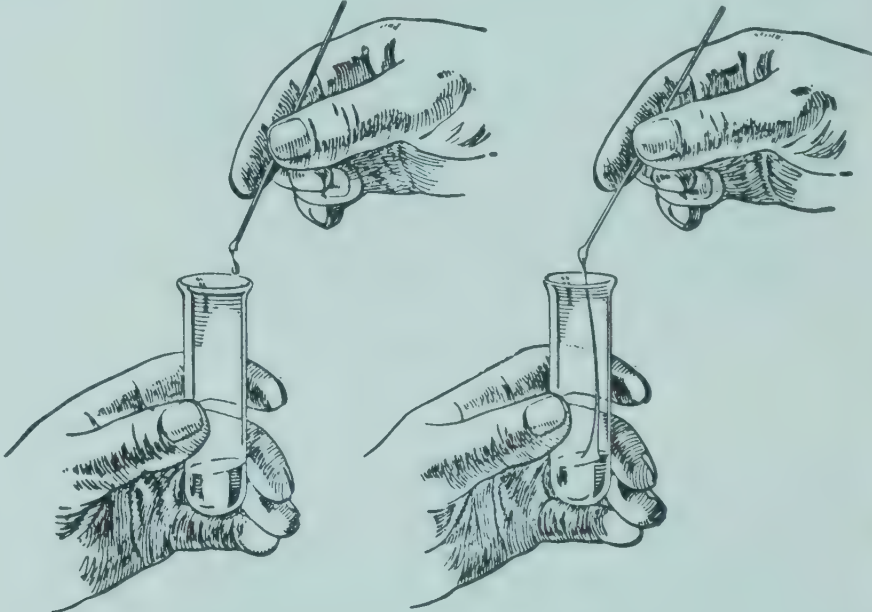


external measurements



Fresh semen

	Normal values	Bibliography	Remarks
Volume of the ejaculate	Mean: 3.39 ml Normal range (mean \pm 2 σ): 0.2–6.6 ml Standard deviation σ : 1.62 ml	MCLEOD, J., <i>Fertility</i> , 2 , 115, 1951 (1000 cases).	After at least 3 days continence. Very variable in the same individual. The volume diminishes on repeated coitus; it can reach 13 ml after long continence. A normal volume appears to be important from the point of view of buffering the acidity of the vaginal secretions; in relation to fertility too great a volume is not a good sign (greater dilution of the spermatozoa and loss due to escape from the vagina). After HOTCHKISS, R. S., <i>Infertility in Men</i> , Springfield, 1952.
Secretions of the glands involved in ejaculation	The volume of the ejaculate is primarily dependent on the secretions of the prostate and the seminal vesicles. The contribution of the COWPER's glands and the epididymis is small, that of the testes (inc. the spermatozoa) even smaller.	HOTCHKISS, <i>Fertility in Men</i> , Philadelphia, 1944; <i>Infertility in Men</i> , Springfield, 1952.	In the course of an ejaculation, 1–2 drops of a clear, colourless liquid, the secretion of the COWPER's glands, first appear. This neutralizes the acidity of the urethra in preparation for the subsequent ejaculation. Then follows first the milky prostate secretion, usually free of spermatozoa, then the part containing the spermatozoa, and finally the gelatinous, highly viscous secretion of the seminal vesicles, often reminiscent of tapioca.
Colour and appearance	Milky-turbid, slightly opalescent, with viscous filaments and grains resembling tapioca. The opalescence is proportional to the spermatozoa concentration.		
Coagulation	Takes place immediately after the ejaculation. The mechanism is unknown. After a few minutes a softening and liquefaction starts and is complete in about 15 minutes with the exception of a number of the tapioca-like grains, which may maintain their consistency up to an hour.		



Normal viscosity Higher viscosity

Semen, 15 minutes and more after ejaculation

Viscosity	6.54 (at 20° C) compared to water = 1	ZAGAMI, V., <i>Arch. Sci. biol.</i> , 25 , 208, 1939.	According to HOTCHKISS the viscosity is of some importance in judging semen, especially when the spermatozoa show reduced vitality and motility. HOTCHKISS describes several simple methods of assessing the viscosity, one of which is illustrated above: the semen is twirled by means of a glass rod in a test tube (at room temperature) and the viscosity tested as shown.
Surface tension	66 dyn cm ⁻¹ 52–59.5 dyn cm ⁻¹ (15° C)	ZAGAMI, <i>loc. cit.</i> SHEDLOVSKY et al., <i>Proc. of the 2nd Conf. on Biology of the Spermatozoa</i> , National Committee on Maternal Health, USA, 1940.	
Hydrogen-ion concentration	pH 7.2–7.39	HOTCHKISS, <i>loc. cit.</i>	When loss of CO ₂ from the sample is prevented. Otherwise the semen will be somewhat more alkaline, ca. pH 7.6–8.0. The motility of the spermatozoa is dependent on the pH value and in contact with the acid vaginal secretion (pH 3.5–4.2) they are rapidly immobilized (see under Volume above). Normally, however, the (fertilizing) spermatozoa hardly come into contact with the vaginal secretion since those deposited at the uterus are rapidly drawn into the upper neck of the cervix (pH 7.8) by the sucking action of the cervix actuated by the orgasm. There they have been observed as little as 3 minutes after ejaculation. The spermatozoa are certainly not capable of such rapid movement under their own unaided motility. This circumstance may explain the diminished capacity for conception generally shown by frigid women.

	Normal values	Bibliography
Specific gravity	1.020–1.040	BELONOSCHKIN, B., <i>Zengung beim Menschen</i> , Stockholm, 1949.
Freezing-point depression	0.56–0.58 after 1 hour 0.74–0.78 after 16 hours	ZAGAMI, V., <i>Arch. Sci. biol.</i> , 25 , 208, 1939.
Electrical conductivity	0.0088–0.0107 S \times cm ⁻¹ * (18° C)	ZAGAMI, <i>loc. cit.</i>

Chemical composition of the seminal fluid (without spermatozoa, unless otherwise stated)

	Normal values mg/100 ml, unless otherwise stated	Bibliography	Remarks
Dry residue	10–20% (1–2% salts, 8–10% organic compounds, 2–6% proteins, 0.21% ether-soluble)	WEISMAN, A. I., <i>Spermatozoa and Sterility</i> , New York, 1941.	
Proteins	1.58–1.80 g	SHEDLOVSKY et al., <i>Proc. of the 2nd Conf. on Biology of the Spermatozoa</i> , National Committee on Maternal Health, USA, 1940.	According to GOLDBLATT, M. W., <i>Biochem. J.</i> , 29 , 1346, 1935, the seminal proteins consist mainly of albumins, globulins (traces), mucin (traces), nucleoproteins and thrombo-plastin, no peptones. According to EVERETT, M. R., <i>Medical Biochemistry</i> , New York, 1946, spermine occurs in concentrations of 90–200 mg/100 ml (in the tissues 1–30 mg/100 g). The spermine originates in the prostate.
Amino-acids (extracted with butyl alcohol)	31–56 mg. equiv/litre	SHEDLOVSKY, <i>loc. cit.</i>	
Residual nitrogen ..	55–80	HUGGINS and JOHNSON, <i>Amer. J. Physiol.</i> , 103 , 574, 1933.	
Urea	72	GOLDBLATT, M. W., <i>Biochem. J.</i> , 29 , 1346, 1935.	
Fructose	50–500	MANN, T., Hormonal Aspects of Carbohydrate Metabolism in Semen and Male Reproductive Organs, in <i>Ciba Foundation Colloquia on Endocrinology</i> , VI, 295, 1953.	The sugar content of semen is very variable and originates mostly from the seminal vesicles. The sugar in semen appears to be important for the metabolism of the spermatozoa, where it is absorbed anaerobically (glycolysis); oxygen is toxic to spermatozoa.
Lactic acid and other organic acids (extracted with ether)	468–603 mg; 52–67 mg. equiv/litre . . . (as lactic acid)	SHEDLOVSKY, <i>loc. cit.</i>	
Lactic acid	36–51 mg; 4.0–5.6 mg. equiv/litre 90–100 according to GOLDBLATT	SHEDLOVSKY, <i>loc. cit.</i>	
Citric acid	80–800	MANN, T., <i>loc. cit.</i>	
Cholesterol	80	GOLDBLATT, <i>loc. cit.</i>	
Phosphorus			
inorganic	40–50	GOLDBLATT, <i>loc. cit.</i>	
total acid-soluble ..	95	GOLDBLATT, <i>loc. cit.</i>	
spermine-P	15–30	GOLDBLATT, <i>loc. cit.</i>	

* S \times cm⁻¹ = siemens \times cm⁻¹ = ohm⁻¹ \times cm⁻¹.

	Normal values mg/100 ml, unless otherwise stated	Bibliography	Remarks
Chlorides (as NaCl) .	230–280 mg; 39–48 mg. equiv/litre ...	SHEDLOVSKY et al., <i>Proc. of the 2nd Conf. on Biology of the Spermatozoa</i> , National Committee on Maternal Health, USA, 1940.	
Calcium	24–25	GOLDBLATT, M. W., <i>Biochem. J.</i> , 29 , 1346, 1935.	
Carbonates (as CO ₂).	41–60 vol%; 18.3–26.9 mg. equiv/litre.	SHEDLOVSKY, <i>loc. cit.</i>	See under pH value, page 276.
Phosphatase			
acid	540–4000 KING and ARMSTRONG units	GUTMAN and GUTMAN, <i>Endocrinology</i> , 28 , 115, 1941.	Originates mainly from the prostate. The phosphatase content is fairly constant in any one individual but varies widely in different individuals. See Prostate secretion, below.
alkaline (pH 9)	0.1–1 KING and ARMSTRONG units		
Hyaluronidase (in semen plus spermatozoa)	100 units	1 unit = that quantity of hyaluronidase in 1 ml of semen (with spermatozoa) which is sufficient to depolymerize 2.5 mg of hyaluronic acid (after McCLEAN, D., <i>Biochem. J.</i> , 37 , 169, 1943, and KURZROK et al., <i>Amer. J. Med.</i> , 1 , 491, 1946).	The concentration of hyaluronidase increases with that of the spermatozoa, although a direct correlation only exists between 50 and 100 millions, i.e. below 50 millions the hyaluronidase content is very small or zero, above 100 millions it no longer increases in proportion to the number of spermatozoa. There is no connection between the hyaluronidase content and the morphology of the spermatozoa.
Formed elements ..	Apart from spermatozoa semen contains the following bodies: giant cells, SERTOLI's cells, epithelial cells, leucocytes, prostate cells, lecithin bodies, BÖTTCHER's crystals, CHARCOT-NEUMANN crystals, fat crystals, spermine phosphate, testicular cylinders, corpora amylacea, mucus and bacteria.	See Prostate secretion, below.

Composition of the prostate secretion

After HUGGINS, C., *Physiol. Rev.*, **25**, 281, 1945

Normal values per 100 ml	Normal values per 100 ml	
pH	Total ether-soluble	Formed elements. <i>Lecithin bodies</i> (small rounded refracting particles up to the size of erythrocytes) which are regarded, however, by SCOTT, <i>J. Urol.</i> , 53 , 712, 1945, as fat granules; <i>corpora amylacea</i> , light yellow to brown spheres, ca. 250 µm diameter, consisting mainly of protein and nucleic acids, and weakly acidophile; <i>epithelial cells</i> ; a few <i>leucocytes</i> ; <i>granulated prostate cells</i> , large, round or irregularly formed, giving the impression that they consist solely of granulations.
Spec. grav. ∴ 1.022	substances ... 62–105 mg	
Water	Cholesterol	
Sodium	Citric acid	
Potassium ...	Acid phosphatase	
Calcium	255–1727 KING	
Chlorides ...	and ARMSTRONG units	
Acid-sol. P ..	Alkaline	
Carbonic acid	phosphatase ..	
Total N	286 K. and A. units	
Residual N..	Vitamin C	
Total proteins	0.54 mg	
Glucose		
	According to HUGGINS and NEAL, <i>J. exp. Med.</i> , 76 , 527, 1942, and HUGGINS and VAIL, <i>Amer. J. Physiol.</i> , 139 , 129, 1943, the prostate secretion also contains fibrinolysin or fibrinogenase.	

Prostate

Phosphatase content of the prostate in KING and ARMSTRONG units

At birth	4.5
4 years	1.5
13 years	73
Adults	522–2284

The phosphatase content of the prostate greatly exceeds that of the liver, bones, kidneys and duodenal mucosa.

The prostate is rich in spermine: EVERETT, M. R., *Medical Biochemistry*, New York, 1946, gives a value of 130 mg/100 g as spermine phosphate. The glucose content is low, the citric acid content relatively high. The acid phosphatase content, according to GUTMAN and GUTMAN, *Proc. Soc. exp. Biol.*, **39**, 529, 1938, and GUTMAN et al., *Amer. J. Cancer*, **28**, 485, 1936, increases with age, as shown in the adjacent table.

Morphology. See the adjacent diagram and the normal and abnormal spermatozoa illustrated on page 281.

Spermatogenesis and vitamins. The relations between these are as yet unexplained. No vitamin has yet been shown to have a (direct) favourable effect, although in severe avitaminosis the spermatogenesis is sympathetically affected.

Spermatogenesis and hormones. Testosterone has a distinctly inhibiting effect on spermatogenesis and is therefore only indicated in cases where the infertility is attributable to underdevelopment of the copulatory organs or to impotence.

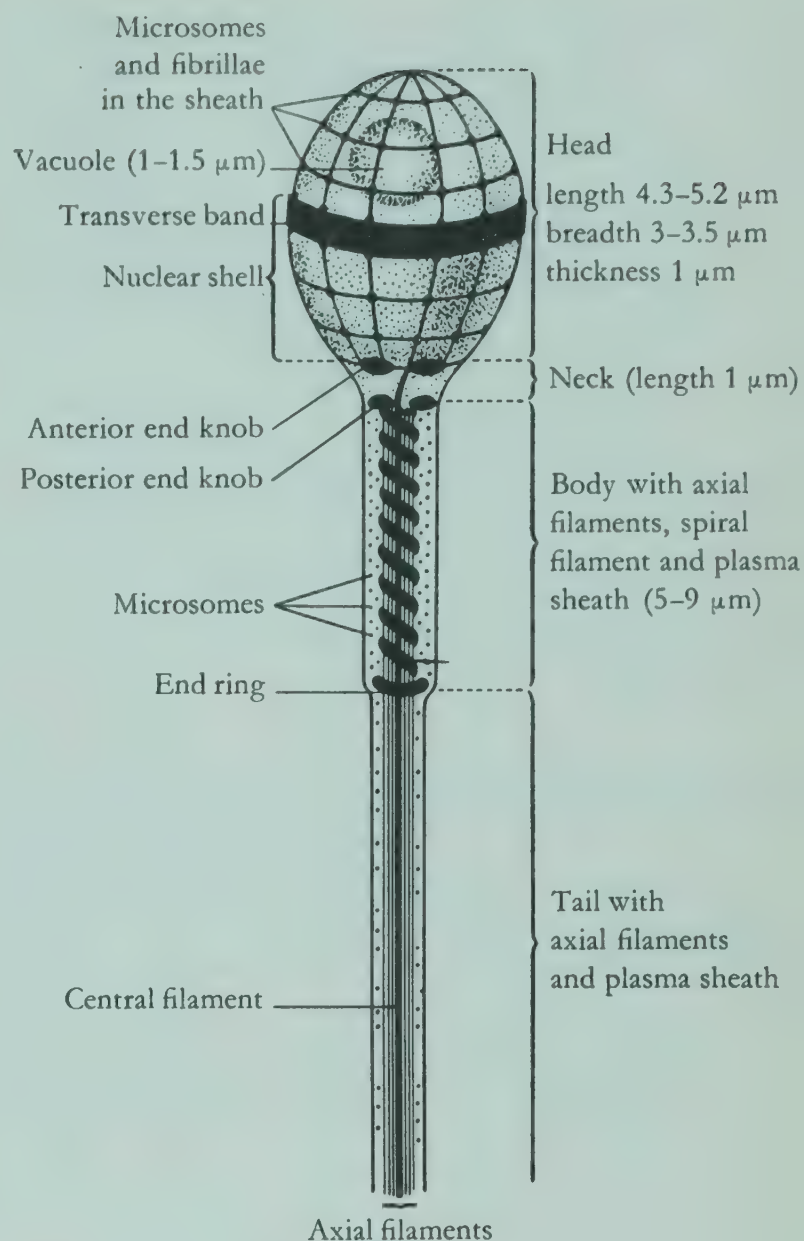
It has recently been observed that several months (up to 16–27 months) after temporary azoospermia provoked by testosterone in oligospermic men, the number of spermatozoa showed a sudden increase (e.g. from 10 millions before treatment up to 170 millions). Cf. HECKEL et al., *J. clin. Endocr.*, 11, 235, 1951; HECKEL and McDONALD, *Fertility*, 3, 49, 1952.

According to HOTCHKISS, *Infertility in Men*, Springfield, 1952, there is no evidence that gonadotropic hormones (pituitary or placental) have any clearly favourable effect. This may perhaps be due to the fact that present-day preparations are still of too low a concentration to produce positive therapeutic results. In cases of hypothyreosis a favourable effect on fertility is shown by thyroxine (or thyrotropic hormone), and a trial is indicated even in cases where there is no obvious disturbance of thyroid function.

Fertility and spermatozoal concentration (see the nomogram on the following page). Although there is no absolute correlation between spermatozoal concentration and fertility (or infertility) the two are probably related insofar as the spermatozoal content of the ejaculate of infertile men is in general lower. In addition, a small ejaculate volume represents an absolute diminution in the number of spermatozoa, an excessive ejaculate volume a lowering of the spermatozoal concentration.

According to KAUFMANN (*loc. cit.*) the normal spermatozoal content amounts to 28–225 millions per cubic centimetre. Many authorities regard 60 millions as the lower limit for a fertile semen. The spermatozoal concentration in any individual can vary greatly and is adversely affected by severe emotional stress and by physical exertion. It is also diminished in certain cases by prolonged continence, which increases above all the proportion of abnormal spermatozoa, and when the temperature of the testes is too high (cause of their degeneration in cryptorchism). Seasonal variations have also been observed (lowered spermatozoal concentration during the warm months) but are statistically insignificant. In assessing the spermatozoal concentration the volume of the ejaculate must also be taken into account.

Fertility and morphology (see the nomogram on the following page). In this respect too there exists only a relative, although distinct, connection; infertile men show on the average a markedly higher proportion of abnormal



After STIEVE, H.,
Handbuch der mikroskopischen Anatomie des Menschen,
Berlin, 1930.

spermatozoa. According to HOTCHKISS, *Fertility in Men*, Philadelphia, 1944, the average spermatozoal composition of semen is as follows:

Form	Mean	Range
Oval or normal	84.1 %	31–98 %
Tapering	9.5 %	0–59 %
Round	1.7 %	0–9 %
Duplicate	1.8 %	0–17 %
Giant and pinhead	0.6 %	0–8 %
Amorphous	2.1 %	0–12 %

KAUFMANN, S. A., *Human Fertility*, 11, 3, 1946, found an average of 89.4% of normal forms in healthy subjects, and the same figure is given by MCLEOD, *Conference on Diagnosis in Sterility*, National Committee on Maternal Health, USA, 1946. According to MOENCH, *Amer. J. Obstet. Gynec.*, 32, 406, 1936, 8.5% of tapering forms represents the limit for a fertile semen.

Motility and longevity. In freshly ejaculated semen the spermatozoa are relatively immotile. As liquefaction proceeds the motility increases and is then maintained constant for 3–5 hours. In the cervical secretion the motility is maintained much longer as a result of the pre-

sence there of substances essential to spermatozoal metabolism which are lacking *in vitro*. Heat increases the motility but reduces the longevity (increased consumption of nutrient reserves owing to increased activity). According to WEISMANN, A. I., *Spermatozoa and Sterility*, New York, 1941, spermatozoa may be classed according to their motility as follows (figures are normal percentages): 1. Immobile (dead) 15%; 2. Only slightly motile 15%; 3. Moderately motile and 4. Very motile, together at least 75%.

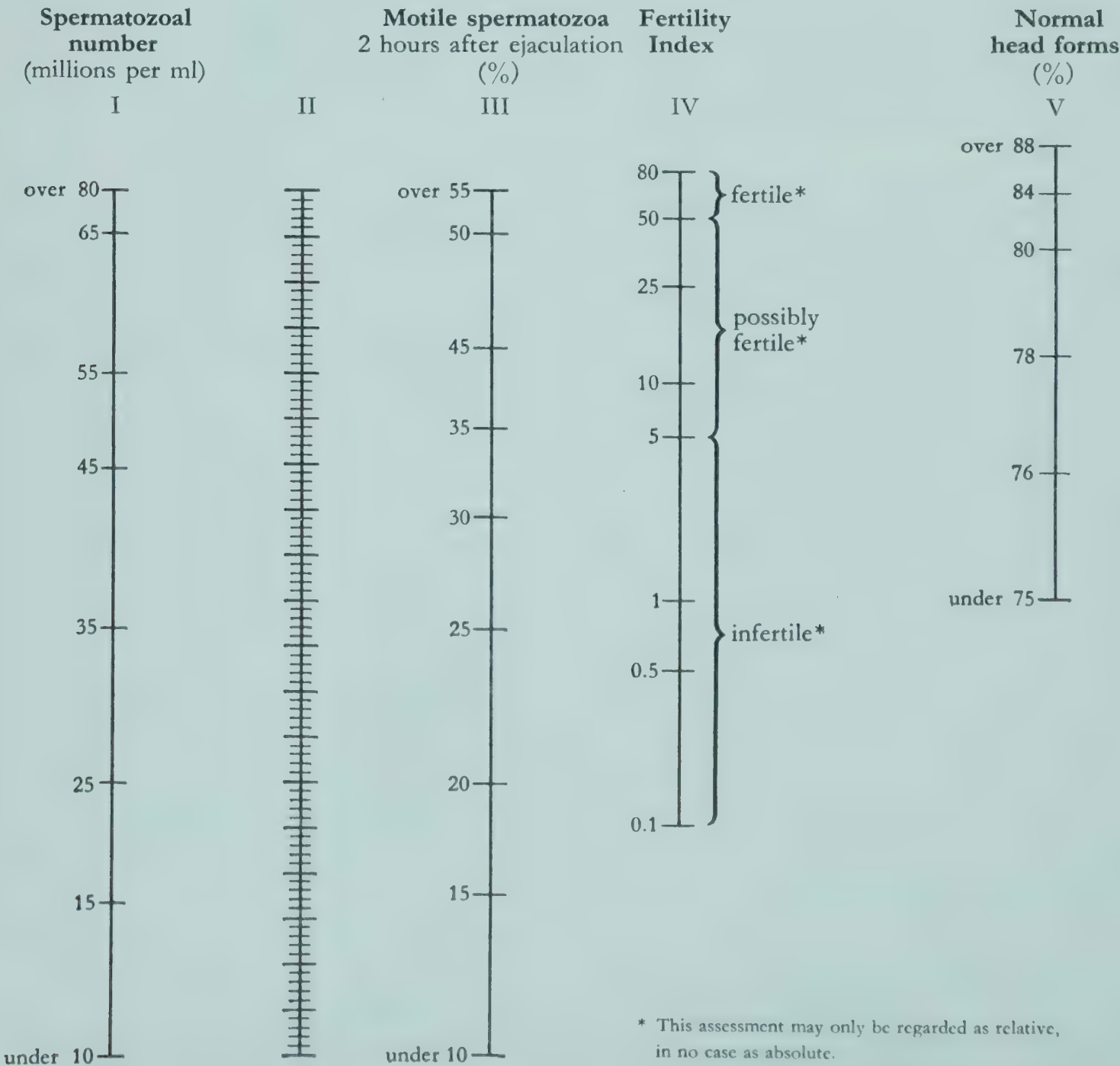
KAUFMANN (*loc. cit.*) gives the following values for the decreasing motility of spermatozoa: normally motile after 3 hours, 61%; after 6 hours, 46%; after 12 hours, 28%.—The decreasing motility is not a measure of decreasing fertility since the latter diminishes more rapidly. *Semen samples collected with the aid of a condom are useless for assessment of motility* since this method has an adverse effect on the mobility.

For the rapid differentiation of living and dead spermatozoa by means of eosin staining, see HEINKE, E., *Z. Haut- u. GeschlKr.*, 10, 254, 1951.

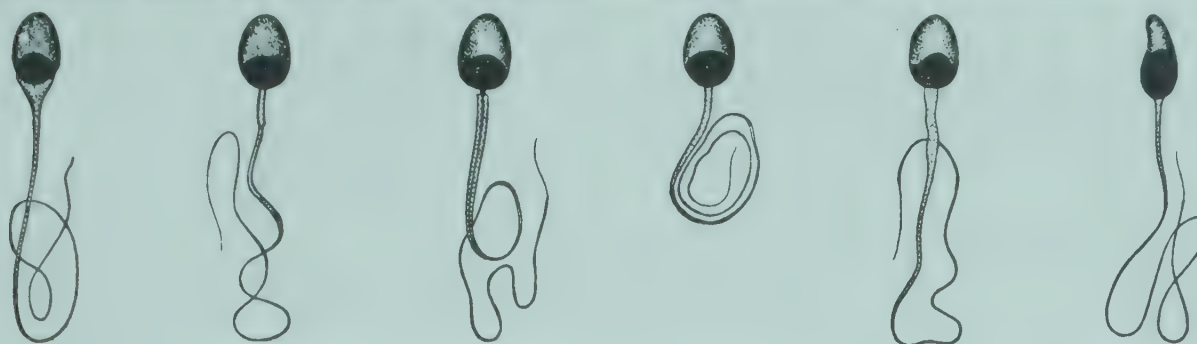
Assessment of fertility. In the present state of knowledge it is impossible to assess absolutely the fertility or infertility of semen except in cases where repeated tests have confirmed azoo- or necro-spermia. However, in the case of sterile unions, where the circumstances are otherwise normal, abnormal values have been repeatedly observed for ejaculate volume and spermatozoal composition and concentration. Greatly increased values for abnormal, poorly motile and immotile and short-lived spermatozoa have also often been observed in such cases. It is therefore highly probable that sterility is here due to the poor quality of the ejaculate.

Nomogram for the assessment of seminal quality on the basis of spermatozoal number, motility and head normality (after PAGE and HOULDING, *Fertility*, 2, 140, 1951)

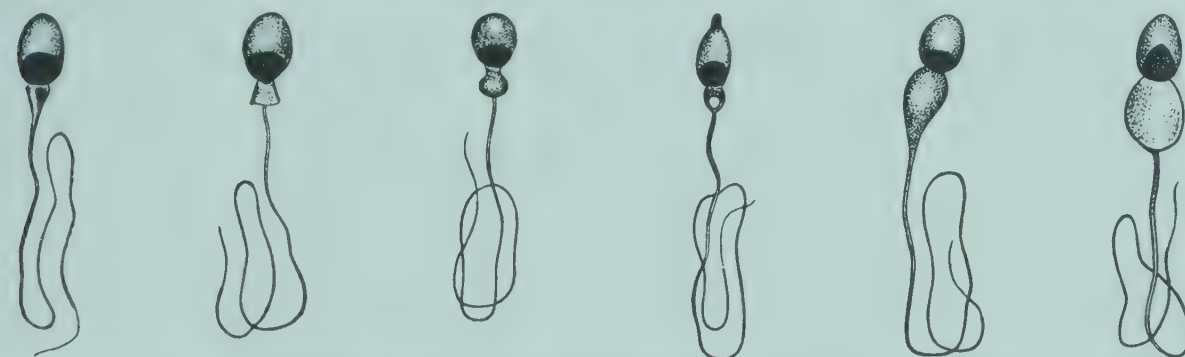
A straight line is drawn between the observed spermatozoal number (on scale I) and the observed percentage of motile spermatozoa (on scale III). The intersection of this line with scale II is now connected by another straight line with the observed percentage of normal head forms on scale V. The intersection of this line with scale IV gives the fertility index.



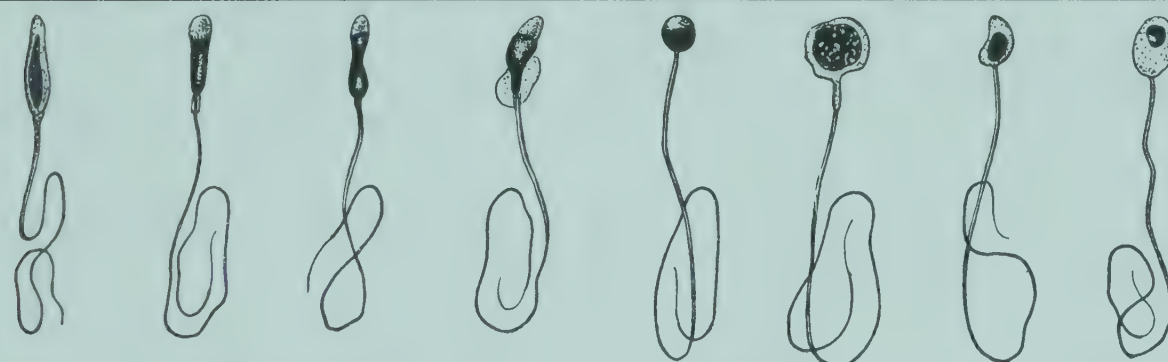
* This assessment may only be regarded as relative, in no case as absolute.



Normal, oval spermatozoa
(side view on the extreme
right)



Normal, oval spermatozoa
with cytoplasmic
appendages



Abnormal spermatozoa
(from left to right):
1–4 tapering forms
5–8 round forms



Abnormal spermatozoa
duplicate forms



Abnormal spermatozoa
giant and pinhead forms



Abnormal spermatozoa
amorphous forms

¹) After HOTCHKISS, R. S., *Infertility in Men*, Springfield, 1952.

The quantity and chemical composition vary markedly with the nature of the excitation causing their production.

Saliva

From the parotid gland, watery secretion; from the submaxillary and other glands, mucous secretion. Specific gravity 1.002–1.008; freezing-point depression 0.2–0.4°C; pH 6.2–7.2. Daily production (man) 1–1.5 litres.

Enzymes: amylase or ptyalin (lipase, proteinase, peptidase originating from leucocytes and epithelium).

100 ml saliva contain:

Water	99.4 g	Calcium (as Ca)	4.9–7.5 mg	Total N	67.1 mg
Dissolved substances	0.5 g	Ratio of sodium to		(Urea + ammonia)-N	11.3 mg
organic	0.12 g	potassium* (in equiv.).	1.3 ± 0.5	Uric acid N	1.5 mg
inorganic	0.2 g	Magnesium	0.7 mg	No sugar	
Mucin and epithelium	0.1 g	Sulphur	7.6 mg		

* In ADDISON's disease the ratio of sodium to potassium rises to 2.2 ± 0.5. If the sodium level in serum is below 132 mg. equiv/litre this increase must not be assumed to be that characteristic of adrenal insufficiency (cf. THORN et al., *Amer. J. Med.*, 10, 595, 1951).

Intestinal juice

Specific gravity 1.010–1.011; freezing-point depression 0.62°C; pH 8.3. Estimated daily production 200 ml. After ingestion of food the pH values in the various parts of the intestine are as follows:

Duodenum	4.7–6.5	Lower jejunum	6.2–7.3
Upper jejunum	6.2–6.7	Ileum	6.1–7.3

Enzymes: erepsin, enterokinase, lipase, amylase, maltase, invertase, lactase, nucleases, etc.

100 ml intestinal juice contain:

Water	98 g	NaCl	0.5 g
Dissolved substances	2 g	NaHCO ₃	0.4 g
Salts	0.9 g	Proteins	0.8 g
Calcium	5–12.8 mg; mean 7.7 mg	Nitrogen	0.035–0.2 g
Phosphorus	4.5–13.2 mg; mean 6.8 mg		

Pancreatic juice

Specific gravity 1.005–1.014; freezing-point depression 0.61–0.62°C; pH 7.5–8.8. Daily production of the order of 1–1½ litres.

Enzymes: trypsin, chymotrypsin, carboxypeptidases, polynucleotidases, lipase (steapsin), amylase (maltase, amylopsin).

100 ml pancreatic juice contain:

Water	98 g	Chlorides ...	6–8 mg. equiv	Residual N	14.3 mg
Dry residue.	2 g	Bicarbonates .	6–7.5 mg. equiv	Urea N	5.0 mg
Ash	0.6–0.7 g	Total protein.	190–340 mg	Uric acid	0.2 mg
Sodium ...	13.8 mg. equiv	Albumins ...	60 mg	No sugar, no cholesterol, no sul-	
Calcium ...	0.22–0.32 mg. equiv	Globulins ...	40 mg	phates, no nucleoproteins	

The alkalinity increases with the duration of the secretion.

Bile

Freezing-point depression 0.54–0.63°C; pH 7.4–7.7; specific gravity: from hepatic duct 1.010–1.012, from gallbladder 1.026–1.032. Daily production 800–1100 ml; pressure of the secretion, 220–270 mm bile (16–20 mm Hg).

Composition in parts per thousand by weight (after HAMMARSTEN)

	Hepatic duct	Gall-bladder		Hepatic duct	Gall-bladder
Water	965	840	Fatty acids and soaps	1.4	10.6
Dry residue	35	160	Cholesterol	1.6	8.7
Mucin and pigment	4.3	44.3	Lecithin	0.6	1.4
Alkali salts of bile acids	18.2	87.2	Fats	0.5	6.0
taurocholates	2.1	19.3	Soluble salts	6.8	3.0
glycocholates	16.1	67.9	Insoluble salts	0.5	2.4

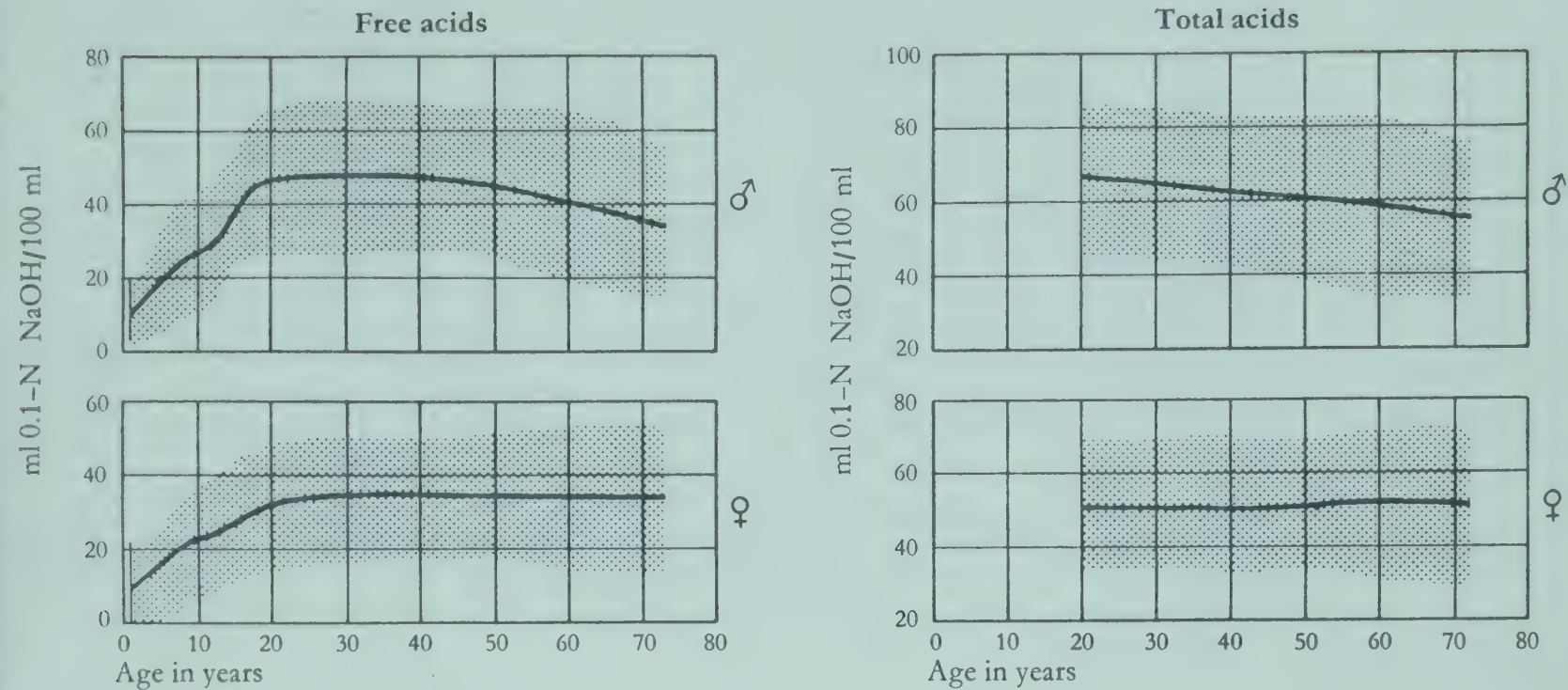
Normal values in fasting, unless otherwise stated

	Normal values	Bibliography	Remarks
Colour	pearl-grey		Sometimes yellowish or greenish as a result of regurgitated bile.
Odour	acid, penetrating		A foetid odour combined with large amounts of food remnants, many leucocytes, blood and organic acids is always pathognomonic.
Blood	traces can occur as a result of trauma following intubation		
Bile	may or may not be present		The presence of bile in fasting gastric juice is of little diagnostic significance, as also 1 hour after the test meal, since intubation often provokes a reversed peristalsis and consequent regurgitation of bile. On the other hand, in fractionated withdrawal no bile should appear after the first withdrawal until the stomach is completely emptied.
Mucus	traces		In excessive swallowing of saliva there is normally an increase in the amount of mucus.
Volume			
Children	0.4–80 ml, 80 % between 0.1–10 ml	WOLMAN, I. J., <i>Amer. J. Dis. Child.</i> , 71 , 394, 1946.	No sex difference.
Adults	30–80 ml		An abnormal volume (150–500 ml) indicates gastric atony of some sort.
	3–5 litres per day	MATTICE, <i>loc. cit.</i>	
Basal secretion			
Children	see the following page		
Adults			
10-minute volume after histamine injection of 0.01 mg/kg	37 ml at 25 years, falling to 24 ml at 65 years		
1-hour volume after EWALD test meal*	50–100 ml	EVERETT, M. R., <i>Medical Biochemistry</i> , New York, 1946.	
Hydrogen-ion concentration	pH 1.2 ± 0.3 (from gastric fistula)		
	pH 1.7 ± 0.1 one hour after EWALD test meal		In children usually somewhat more alkaline.
Specific gravity	1.010–1.0036	REHFUSS, M. E., <i>Diagnosis and Treatment of Diseases of the Stomach</i> , Philadelphia, 1927.	
Freezing-point depression	0.816–0.298° C		
Total acids in ml 0.1-N NaOH required to neutralize 100 ml	2–80, usually 10–50	HARRISON, G. A., <i>Chemical Methods in Clinical Medicine</i> , London, 1947.	See the following pages.
Free hydrochloric acid in ml 0.1-N NaOH/100 ml	0–70, usually 0–30	HARRISON, <i>loc. cit.</i>	See the following pages.
Lactic acid	0		
Chlorides (as Cl)	550 mg/100 ml		
Uric acid	0.8–2.0 mg/100 ml		
Residual nitrogen	20–48 mg/100 ml	MATTICE, M. R., <i>Chemical Procedures for Clinical Laboratories</i> , Philadelphia, 1936.	
(Urea + ammonia)-N	7–14 mg/100 ml		
Amino-N	2–8 mg/100 ml		
Enzymes	pepsin, cathepsin (proteases); lipase (esterase) in adults 0 or traces, but present throughout childhood		There is no particular lab enzyme. Milk is coagulated by the enzyme action of pepsin and also by gastric juice. Pepsin and cathepsin are present in the ratio of about 1:1. Pepsin has optimal activity at pH 1.8, cathepsin at pH 3.8. See the following page.

* EWALD test meal: 2 slices of dry bread + 250–350 ml (2 glasses) of water.

Normal range and mean for free and total acids

After VANZANT et al., *Arch. intern. Med.*, 49, 345, 1952



Normal mean and standard deviation for free and total acids, volume and achlorhydria in adults

After VANZANT, ALVAREZ, BERKSON and EUSTERMAN, *Arch. intern. Med.*, 52, 616, 1933
(3764 normal subjects, test meal of 400 ml water and 8 arrowroot biscuits)

Age	Men								Women							
	Free acids ¹		Total acids ¹		Volume ml		Achlorhydria %		Free acids ¹		Total acids ¹		Volume ml		Achlorhydria %	
	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation	Absolute	Apparent	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation	Absolute	Apparent
20-24	46.7	16.5	63.5	16.5	118.0	49.5	32.0	14.5	49.7	14.5	100.5	39.0	2.0	3.0
25-29	47.0	17.0	63.0	16.2	116.5	50.5	2.0	33.0	14.0	50.0	14.2	100.0	39.0	4.5	6.5
30-34	47.0	16.7	62.5	16.2	113.5	50.0	3.0	5.2	33.0	13.7	50.5	14.7	99.0	39.0	7.3	10.0
35-39	47.0	16.5	61.7	16.4	109.5	48.5	6.3	8.5	33.0	14.0	50.5	15.1	97.7	39.0	10.0	13.5
40-44	46.5	16.5	60.7	17.2	105.0	46.0	9.5	11.7	33.0	13.8	50.5	15.2	96.0	39.0	12.7	17.0
45-49	45.5	16.7	59.5	18.4	101.0	43.0	12.7	15.0	33.0	13.5	50.5	14.2	94.0	38.5	14.5	20.5
50-54	43.7	17.6	58.3	19.1	97.5	41.0	16.0	18.5	33.0	14.0	50.5	14.7	92.0	37.5	18.2	24.0
55-59	41.5	18.7	57.0	19.2	95.0	42.0	19.3	21.5	33.5	15.0	50.5	15.3	89.5	37.0	21.0	27.5
60-64	39.3	19.4	55.5	18.8	93.5	45.0	22.0	25.0	33.5	16.0	50.5	16.0	87.0	36.0	23.5	31.0
65-69	37.3	18.5	53.7	17.5	92.0	47.0	22.5	26.0	33.5	16.0	50.5	16.7	84.0	35.0	26.3	31.5
70-79	33.5	17.0	50.5	16.7	91.0	50.5	17.0	21.0	33.5	15.2	50.5	17.2	79.0	33.0	24.0	28.7

Normal values for basal secretion per minute, free and total acids in children after histamine stimulation

After WOLMAN, I. J., *Amer. J. med. Sci.*, 207, 782, 1944

Age	Basal secretion per min. ml	Free acids ¹	Total acids ¹	pH
Premature births	0.12-0.15	0	0- 8	4.7
Newborn	0.20-0.45	0- 20	15- 40	2.3-3.6
2 weeks to 6 months	0.25-1.10	0- 59	5- 71	1.5-3.4
7-12 months	0.40-1.50	12- 80	25-105	1.5-2.2
1-2 years	0.70-1.80	15- 95	26-106	1.2-2.0
2-5 years	0.50-2.20	20- 90	38-102	1.4-2.0
5-10 years	0.10-3.30	53-113	61-145	1.4-2.0
10-15 years	2.70-3.60	49-115	61-128	1.4-2.0

Age and gastric proteases

After BUCHS, quoted by FREUDENBERG, E., *Verdaunungsphysiologie des Kindes*, in FANCONI and WALLGREN, *Lehrbuch der Pädiatrie*, Basle, 1954

	Infants	Children 1-5 years	Children 6-15 years	Adults
1 enzyme unit is contained in (ml)	0.8-3	0.4-1.2	0.2-0.6	
Average	1.5	0.7	0.3	
Enzyme units per ml gastric secretion (average) ..	0.7	1.5	2-4	
Ratios	1	2	5	
Daily production of enzyme units	200 × 0.7 = 140	500 × 1.5 = 750	1000 × 3 = 3000	1500 × 4 = 6000
Ratios	1	5	20	40

¹) In ml 0.1-N NaOH/100 ml.

Data in health and in various pathological conditions

After HARRISON, G. A., *Chemical Methods in Clinical Medicine*, London, 1947

	Normal		Ulcus ventriculi		Duodenal ulcer		Gastric carcinoma		Chronic dyspepsia and/or gastritis		Pernicious anaemia	
	ml 0.1-N NaOH/100 ml	g/100 ml as HCl	ml 0.1-N NaOH/100 ml	g/100 ml as HCl	ml 0.1-N NaOH/100 ml	g/100 ml as HCl	ml 0.1-N NaOH/100 ml	g/100 ml as HCl	ml 0.1-N NaOH/100 ml	g/100 ml as HCl	ml 0.1-N NaOH/100 ml	g/100 ml as HCl
Free acids	0- 70	0.00-0.26	0- 70	0.00-0.26	0- 95	0.00-0.35	0- 70	0.00-0.25	0- 70	0.00-0.25	0	0.00
Total acids	5-100	0.02-0.36	10-100	0.04-0.36	15-110	0.05-0.40	3- 80	0.01-0.29	3- 55	0.01-0.20	0-40	0.00-0.15
Total chlorides	55-110	0.20-0.40	50-120	0.18-0.44	70-130	0.25-0.48	20-110	0.08-0.40	45- 90	0.17-0.33	—	—
Inorganic chlorides	20- 50	0.07-0.18	10- 55	0.04-0.20	10- 65	0.04-0.24	10- 65	0.04-0.24	15- 65	0.05-0.24	—	—
Remarks on the acid values ..	Achlorhydria is normal in 4%, hyperchlorhydria in 10% of cases. The achlorhydria usually increases with age.		No characteristic values.		Usually hyperchlorhydria, hyperacidity and high total chlorides.		Usually achlorhydria, hypoacidity and low total chlorides.		No characteristic values.		100% achlorhydria, usually low acid and chloride values.	
Lactic acid	0		0		0		0 or +		0 or +		0 or +	
Blood	0 or + (trauma)		0 or +		0 or +		0 or +		0 or +		often +	
Bile	0 or +		0 or +		usually +		0 or +		0 or +		0 or +	
Volume	20-100		40-150		30-110		10-500		20-200		5-50	
Leucocytes	+		+ to ++		0 to +		+ to +++		+ to +++		+ to +++	
Erythrocytes	0 or + (trauma)		0 to +++		0 to +		0 to +++		0 to +		+ to +++	
Epithelial cells	0		0 to ++		0 to +		+ to +++		+ to ++		+ to ++	
(excluding squamous)												
Tumour cells	0		0		0		0 or +		0		0	
Sarcinae	0		0 to +		0		0 to +++ , usually 0		0 to ++		0	
BOAS-OPPLER bacilli	0		0		0		0 to +++		0 to +		0	
Yeast (from test meal)	+		+		+		+		+		+	
Starch (from test meal)	+		+		+		+		+		+	
Cellulose residues	0		0 to +		0		0 to +++		0 to +++		0	

Stomach emptying time and total acidity for various foodstuffs

After HAWK et al., *Practical Physiological Chemistry*, New York, 1937

Foodstuff 100-g portions, unless otherwise stated	Number of observations	Mean of max. total acidity ml 0.1-N NaOH/100 ml	Mean emptying time	
			hours	minutes
Bread and cereals	25	120	3	00
Cakes	29	90	3	00
Eggs and egg dishes	90	80	2	40
Ice cream	7	105	3	15
Meat				
Fish	75	130	2	50
Chicken	20	125	3	15
Veal	7	140	2	50
Beef	25	120	3	00
Mutton	14	135	3	00
Pork	31	120	3	15
Turkey	2	140	3	30
Jellies (fruit-)	5	70	2	00
Vegetables	124	75	2	15
Water ices	4	65	2	35
Yoghurt	4	65	2	25
Tarts	29	90	2	30
Milk				
cow's, 400 ml	50	100	2	30
cow's, 75 ml	3	45	1	15
human, 150 ml	5	60	1	40
human, 225 ml	2	90	2	25
Nuts (25-50 g)	22	100	3	30
Milk puddings	23	90	2	20
Sugar and confectionery (candy)	28	70	2	05

Adults

Daily quantity: mixed diet	160	–	250 g
vegetable diet			370 g
meat diet	54	–	64 g
prolonged fasting	9.5	–	22 g
pathological	500	–	1200 g

Children	4	–	120 g
----------	---	---	-------

Hydrogen-ion concentration:

Usually alkaline or neutral, but is dependent on the diet, on the rate of passage through the intestine, on the intestinal flora, etc. Variations of pH 4.6 to pH 8.8 have been observed in healthy subjects.

Composition:

Cellulose	2 %	} of dry substance
Muscle fibres, nitrogeneous food residues	2 %	
Saponified and unsaponified fats	6 %	
Food residues	10 %	
Bacteria	8 %	}
Salts, mucus, stercobilin	7 %	
Solid matter	25 %	}
Water	75 %	

Average number of stools per day in infants (after GONCE and LEWIS, *Am. J. Dis. Child.*, 80, 274, 1950).

Days	Breast milk	Cow's milk	Irradiated dried milk
1	3.8	3.1	2.9
2	4.0	4.0	5.0
3	4.9	4.9	5.3
4	5.3	5.5	6.6
5	5.4	5.3	6.0
6	4.8	5.1	4.4
7	3.9	4.2	5.2
8	4.1	4.1	4.6
9	3.9	3.8	4.5
10	3.8	4.1	3.6
11	3.7	3.3	4.1
12	3.0	3.4	3.9
13	2.8	3.1	3.7
14	2.7	3.0	3.7
Weeks			
3	2.53	2.70	3.01
4	2.28	2.51	2.99
5	2.06	2.33	2.71
6	1.84	2.16	2.45
7	1.47	2.08	2.40
8	1.24	1.99	2.19
9	1.40	1.84	2.12
10	1.10	1.80	2.08
11	1.15	1.69	2.03
12	1.15	1.69	1.95
13	1.19	1.66	1.93

Nitrogen:

The **nitrogen content** amounts to ca. 0.25 g/day (food residues, bacteria, desquamated epithelium, exudate of the intestinal mucosa). In illness the N-content is often greatly increased (incomplete digestion, poor resorption). High values are mainly found in some diarrhoeas and in pancreatic diseases.

Total fats	7.3–27.6 %	} of dry substance
Neutral fats	2.5–11.8 %	
Free fatty acids	1 –10 %	

Salts and minerals¹

Substance	Average total excretion per day	Comparative amounts excreted in urine and in faeces	
		Urine % of total excretion	Faeces % of total excretion
Chlorides	0.09 g	98	2
Lead	0–0.4 mg	—	—
Potassium	0.47 g	79	21
Calcium	0.64 g	12	88
Magnesium	0.20 g	31	69
Sodium	0.12 g	95	5
Phosphorus	0.51 g	57	43
Sulphur	0.13 g	83	17

Urobilinogen² 20–220 mg/100 g

Colour:

Normal: brown, mainly due to stercobilin; darker on low-residue meat diets, lighter on high-residue vegetable diets. Darkens on exposure to air (oxidation of urobilinogen to urobilin). **Golden yellow** in breast-fed infants (unchanged bilirubin). **Green** colour is due to chlorophyll (spinach) or biliverdin (change in infants' stools). **Black** colour is due to plant juices (bilberry), cabbage, iron (iron sulphide). **Pitch-black** colour is due to high haematin content (consumption of black pudding, haemorrhage of stomach or upper intestine). **Light grey** colour is due to undigested fats following inadequate bile secretion (neutral fats, calcium soaps).

Effects of drugs on the colour of faeces:

Drug	Dose causing abnormal colour	Colour
Bismuth	5 g	Black
Calomel	130–140 mg	Green
Iron	65–70 mg	Grey-black, darkening in air
Methylene blue	130–140 mg	Blue, especially on contact with air
Manganese dioxide	130–140 mg	Dark brown to black
Haematoxylin	1 g	Reddish brown
Rhubarb extract	2 ml	Yellow
Senna extract	4 ml	Deep yellow
Santonin	65–70 mg	Deep yellow

¹) After SHOHL, A. T., *Mineral Metabolism*, American Chemical Society Monographs, No. 82, New York, 1939.
²) After STEIGMANN and DYNIEWICZ, *Gastroenterology*, 1, 743, 1943.

Normal values in grams (unless otherwise stated) in 24-hour urine on a normal balanced diet

Volume (from Mitchell-Nelson Textbook of Pediatrics, Philadelphia, 1950)		Normal values	Methods and bibliography	Remarks
Age	ml			
1-2 days	30- 60	Dilution test (VOLHARD's test) (normal values) Single intake of 1000 ml water, followed by a dry diet. The figures in the left-hand column are hours after the water intake.		Volumes of less than 500 ml or more than 2000 ml are almost always pathological.— <i>Temporary decrease</i> after long thirsting, <i>temporary increase</i> in emotional excitation and after increased liquid intake.
3-10 days	100- 300			<i>Prolonged diminution (oliguria)</i> in certain acute and chronic renal diseases, fever, severe diarrhoea, accumulation of exudates and transudates, cardiac insufficiency. <i>Prolonged increase (polyuria)</i> in diabetes, granular atrophy, prostate hypertrophy, pyelitis, resorption of oedemas, pleuritic and peritoneal effusions.
10 days - 2 months	250- 450			The <i>specific gravity</i> is lowered by abundant liquid intake and by emotional excitation, <i>increased</i> by reduced liquid intake, muscular exertion, profuse sweating and in diarrhoea. Maintenance of a spec. grav. of 1.010 on a dry diet is a sure sign of renal insufficiency.
2 months - 1 year	400- 500			
1- 3 years	500- 600			
3- 5 years	600- 700			
5- 8 years	650-1000			
8-14 years	800-1400			
over 14 years	1000-1600			
or ca. 1 ml per minute				
Specific gravity				
Adults on a normal diet		1.016-1.022		
Newborn during the first few days		1.012		
subsequently		1.002-1.006		
Dry residue		55-70		
Freezing point		-1° C to -2.5° C		
Hydrogen-ion concentration		pH 4.8-7.4; mean pH 6.0		
Nitrogen				
Nitrogenous constituent	g	As nitrogen range g	mean ¹ g	N-content of the constituent as % of total N
Urea ²	20-35	9.4-16.45 .	10.5	84
Uric acid ²	0.1-2.0	0.033-0.66	0.23	1.8
Other purine bases ²	0.02			
Creatinine ²	1-1.5	0.37-0.55 .	0.55	4.4
Creatine ²	0-0.06			
Ammonia ²	0.5-1.0	0.41-0.82 .	0.57	4.6
Amino-acids ² , total	1.1	0.4-1.0 . . .	0.5	4
Amino-acids ² , free	0.5		0.1	0.8
Hippuric acid	0.7		0.055	0.4
Iminazole derivatives	0.015-0.06			
Phenols	0.1-0.3			
Glycocyamine	0.03	0.01	0.01	
Allantoin	0.01-0.025	0.01	0.01	
Indican	0.004-0.02			
Proteins	0.003-0.06			
Total nitrogen		10-18	12.5	100

¹) After EVERETT, M. R., *Medical Biochemistry*, New York, 1946. ²) The excretion of all these substances is increased during therapy with corticotropin, hydrocortisone or cortisone as a result of the anabolic action of these hormones.

Normal values in grams (unless otherwise stated) in 24-hour urine on a normal balanced diet

Amino-acid excretion in mg/24 hours for 18 persons on a normal diet, after HIER, S. W., *Trans. N. Y. Acad. Sci.*, 10, 281, 1948

	Free (mg)		Total (mg)		Combined (mg)		Combined acids as % of total	
	Range	Mean	Range	Mean	Range	Mean	Range	Mean
Arginine	11.0- 36.2	21.3 ± 6.9	12.2- 45.0	23.7 ± 7.9	0 - 13.8	6.6	0 - 52.9	24.2
Aspartic acid	0 - 23.6	1.3 ± 0.6	87.4-258.8	164.5 ± 46.7	82.7-258.8	163.2	82.1-100	99.2
Cystine	45.2-138.0	87.7 ± 25						
Glutamic acid	0 - 63.7	35.8 ± 19.2	102.4-769.5	351.4 ± 151.4	72.6-708.7	315.6	79.0-100	89.8
Histidine	60.3-378.0	188.3 ± 99.2	65.4-438.8	203.3 ± 101.1	5.1-123.2	40.5	4.8- 34.5	14.9
Isoleucine	0 - 20.1	5.9 ± 4.5	11.8- 33.4	20.3 ± 5.5	3.9- 30.3	14.4	18.3-100	71.0
Leucine	3.8- 18.5	9.6 ± 3.3	11.9- 40.0	21.2 ± 6.6	3.5- 29.6	12.3	29.4- 81.8	55.6
Lysine	18.2- 88.2	33.6 ± 16.9	35.6-166.0	73.2 ± 29.4	15.4- 77.8	43.0	23.4- 74.8	57.1
Methionine	4.1- 13.5	7.8 ± 2.9	4.1- 15.0	8.6 ± 2.8	0.5- 6.3	2.3	4.7- 60.5	24.6
Phenylalanine	7.5- 34.0	16.4 ± 7.1	10.3- 45.4	23.3 ± 7.9	3.1- 16.9	8.4	14.4- 66.6	35.2
Proline	3.7- 14.8	8.5 ± 2.9	23.1- 62.1	42.8 ± 12.9	18.1- 54.4	34.3	65.1- 89.0	80.2
Threonine	12.4- 49.5	24.4 ± 10.9	14.8- 84.4	53.8 ± 19.5	18.8- 53.8	31.3	41.7- 67.9	58.0
Tryptophan	8.5- 56.0	24.6 ± 11.3	11.2- 86.1	41.4 ± 17.5	0.6- 28.3	18.4	1.3- 71.8	41.9
Tyrosine	10.5- 43.9	20.8 ± 1.7	23.4-100.3	52.5 ± 18	5.9- 60.3	31.7	25.2- 75.1	60.4
Valine	0 - 7.5	4.5 ± 2.2	11.0- 30.0	19.8 ± 5.6	6.1- 28.2	15.3	55.4-100	77.3

For microbiological assay of amino-acids see, *inter alia*, SCHIYSON, TORGHELE and ANDERSON, *J. Lab. clin. Med.*, 35, 640, 1950.

Reducing substances*

Normal values

Methods and bibliography

Remarks

"Sugar", total	0.5-1.5	Qualitative: FEHLING's test; TROMMER's test; NYLANDER's test; BENEDICT's test; BÖTTGER's test; see also page 294.	Renal glycosuria (with or without evidence of kidney disease); glycosuria resulting from endocrine disturbances; glycosuria in infections and septicaemia; glycosuria in increased intracranial pressure (meningitis, tumours, haemorrhages); glycosuria in ACTH-adrenocortical hormone therapy (cf. page 187).
Glucose	0.5	Quant. (plus fructose): BENEDICT's fermentation test; BERTRAND's test; polarimetrically. Qual.: with phenylhydrazine (phenylosazone test).	*Other constituents apart from glucose with reducing effect: uric acid, creatinine, glucuronic acid (after drugs containing anti-febrin, antipyrine, pyramidone, camphor, chloroform, chloral, morphine, menthol, naphthol, phenol, thymol or turpentine, as also in putrefaction of intestinal contents: glucuronic acid is formed by the liver as detoxicant), salicylic acid (after exhibition of salicylic acid), homogentisic acid (in alkaptonuria), fructose, lactose, pentoses, formaldehyde (after methyl alcohol poisoning). Normally, however, these substances are only of significance in assessing "sugar" content when the content of reducing substances is very small.
Fructose	none or trace	Qual.: SELIVANOFF's test, BANG's test. Quant.: STREPKOV, <i>Biochem. Z.</i> , 287, 33, 1936.	
Lactose	Present in urine in late pregnancy and during lactation, especially in cases of milk retention.	Qual.: RUBNER's test; WÖHLK's test. Quant.: KUROYA, <i>Biochem. Z.</i> , 235, 445, 1931.	
Pentoses	none or trace	Qual.: BIAL's test. Quant.: SUMINOKURA, <i>J. Biochem.</i> , 14, 343, 1931.	
Glucuronic acid*	Qual.: TOLLENS' test. Quant.: FÜRTH and PESCHEK, <i>Biochem. Z.</i> , 287, 376, 1936.	
Acetone bodies			
(1) Total (as acetone)	0.02-0.05	Qual.: 1 + 2, nitroprusside tests (LEGAL's, ROTHERA's). Quant.: 1, 2 and 3, VAN SLYKE's test, MESSINGER-HUPPERT test.	Excretion of acetoacetic acid is increased in starvation, on a completely carbohydrate-free diet, occasionally in febrile diseases and digestive disturbances. In large quantities only in diabetes mellitus. Acetone is formed from acetoacetic acid and is therefore always present in urine containing the latter. β -Hydroxybutyric acid also almost always accompanies acetone and acetoacetic acid. In pathological conditions ketonuria is only of significance when more than 2 g acetone bodies are excreted in 24 hours (ketosis).
(2) Acetone + acetoacetic acid (as acetone)	0.03-0.015	Qual.: GERHARDT's test, ARREGUINE's test.	
(3) β -Hydroxybutyric acid (as acetone)	0.02-0.03	Quant.: polarimetrically.	
Lipids**	0	The urine is mixed with caustic soda and extracted with ether.	Urine has a milky appearance in chyluria (e.g. in filariasis, in diseases of the lymph channels and thoracic duct). Beware of addition of milk by the patient. Lipuria can also occur without chyluria, occasionally for example through rupture of a cyst in the urinary passages, through fractures of the large bones, in chronic nephritis with advanced fatty degeneration of the kidneys, in phosphorus poisoning, in eclampsia, in diabetes mellitus with lipaemia. In lipuria without chyluria the fat is not so finely distributed in the urine and the appearance is less milky.
Free fatty acids	0.008-0.05	SMITH and KIRK, <i>J. biol. Chem.</i> , 103, 391, 1933.	

Refers to the opposite page: According to FORSHAM, THORN et al., *J. clin. Endocr.*, 8, 15, 1948, the uric acid/creatinine ratio is a reliable criterion of adrenocortical function. After 25 mg ACTH it rises 62-130%, on the average 91%. In ADDISON's disease the increase averages 16%, range -14 to +58%. According to TAUSSKY et al., *Proceedings of the Second Clinical ACTH Conference*, Vol. 1, 273, 1951, the ratio also increases markedly in starvation but not so strongly as after ACTH. In fasting the urine contains not only more uric acid but also more citric acid, ascorbic acid and creatinine. As a result of this nutritional dependence the change in uric acid/creatinine ratio after ACTH is now only rarely used as a test of adrenocortical function; a preliminary condition is the constant administration of large amounts of purine-forming substances.

Oxalic acid	0.015-0.02	
Citric acid	0.15-0.3	NATELSON et al., <i>J. clin. Invest.</i> , 27, 446, 1948.

* See under Remarks above, 2nd paragraph.

** The term lipids here means the total matter soluble in ether-alcohol, i.e. neutral fats, fatty acids, waxes, steroids, phosphatides, etc.

Normal values in **grams** (unless otherwise stated) in **24-hour urine** on a normal balanced diet

Normal values		Methods and bibliography	Remarks
Homogentisic acid ...	0	Reduces FEHLING's solution but is optically inactive and unfermentable. Gives a transient blue coloration with ferric chloride.	Present in <i>alkaptonuria</i> . The urine turns slowly dark brown in air and leaves brown stains on underwear. Alkaptonuria is often congenital, of long duration, often lifelong, but not pathognomonic.
Chlorides			
as NaCl	10-15	<i>Quant.</i> : CHRISTY and ROBSON, <i>Biochem. J.</i> , 22 , 571, 1928. See also under Blood, page 326.	<i>Reduced</i> on a diet low in salt, in inanition; in fever (very marked in lobar pneumonia); in accumulation of transudates and oedemas (in kidney diseases, cirrhosis of the liver, cardiac diseases, burns). <i>Increased</i> during resolution of a pneumonia and resorption of transudates and oedemas.
as Cl	6-9		
Sulphates (as SO₃)			
Inorganic	1.4-3.3	Determination of the individual fractions after precipitation as BaSO ₄ . See also under Blood, page 326.	<i>The inorganic sulphur content is lowered</i> after poisoning since the body utilizes sulphates in detoxication. The inorganic S then appears in the alkylsulphuric acid fraction, which is increased after poisoning.
Alkylsulphuric acids (conjugated or esterified sulphuric acids)	0.1-0.25		
Neutral (organic S)	0.15-0.4		
Total	1.6-3.6		
Phosphates, total ...		<i>Qual.</i> : a slight excess of ammonia is added to the urine, followed by magnesia mixture. The resulting precipitate is soluble in acids. If the urine already shows a milky turbulence due to phosphates the test consists simply in the addition of acetic acid: clearing of the turbulence indicates phosphates.	<i>Phosphaturia</i> often occurs in neuropathy; abundant sediment of calcium and magnesium phosphates and carbonates. Due to unusually high excretion of calcium and not a sign of increased excretion of phosphoric acid.
organic	0.5		
Sodium (as Na)	4-6	WANG, C. C., <i>J. biol. Chem.</i> , 111 , 443, 1935.	In fever the amount of Na excreted is diminished, while the K excretion is increased 3-7 times. Cf. page 287.
Potassium (as K)	2.5-3.5		
Calcium (as Ca)	0.01-0.3	After BERNSTEIN and SIMKINS, <i>J. Lab. clin. Med.</i> , 26 , 521, 1940.	Cf. page 287.
Lime (CaO)	0.16		
Magnesium (as Mg)	0.172-0.285; mean 0.206	THOMPSETT, <i>Biochem. J.</i> , 28 , 1536, 1934.	Lime is mainly excreted in the faeces (0.3-0.5 CaO per day). See page 287. Cf. page 287.
Iron (as Fe)	0.0006-0.002		
Amylase (diastase) ..	8000-30,000 units	WOHLGEMUTH	The values of the <i>diastase index</i> correspond to <i>Wohlgemuth units per ml</i> . Normal values 2-50, over 50 suspicious, 100 and over definitely pathological. Mainly in obstruction of the pancreatic duct or acute pancreatitis. In chronic pancreatitis or pancreatic carcinoma normal or lowered, also in kidney diseases. Increased in eclampsia.
For content per ml, see Remarks			
Hormones	see under Hormones	Androgens	page 201
		Corticosteroids	page 182
		Gonadotropic hormones ..	page 179
		17-Ketosteroids	page 200
		Oestrogens	page 201
		Progesterone (Pregnanediol)	page 202
Vitamins		Normal values in milligrams/24 hours	
Fat-soluble vitamins (A, D, E, K)		0-trace	
<i>p</i> -Aminobenzoic acid		0.13-0.2; mean 0.15	
B₁ (aneurine) free		0.01-0.21; mean 0.1	
as cocarboxylase		0.0-0.18; mean 0.04	
B₂ (riboflavin)		0.5-0.8	
Biotin		0.0275-0.0356; mean 0.0317	
C		0.015-0.05	
Choline		5.6-9.0	
Folic acid		0.002-0.004	
Inositol		15	
Nicotinic acid, free		0.25-1.26	
as nicotinamide		0.6-4.0	
as N ¹ -methylnicotinamide		3.2-12.6	
Pantothenic acid		2.5-5	
		Bibliography	
		ROBINSON, F. A., <i>The Vitamin B Complex</i> , London and New York, 1951.	
		KRAUT et al., <i>Biochem. Z.</i> , 308 , 309, 1941.	
		KRAUT, <i>loc. cit.</i>	
		STRONG et al., <i>J. biol. Chem.</i> , 137 , 363, 1941.	
		ROBINSON, <i>loc. cit.</i>	
		STORVICK and HAUCK, <i>J. Nutrition</i> , 23 , 111, 1942.	
		LUECKE and PEARSON, <i>J. biol. Chem.</i> , 153 , 259, 1944.	
		STEINKAMP et al., <i>Proc. Soc. exp. Biol. Med.</i> , 62 , 556, 1946.	
		JOHNSON et al., <i>J. biol. Chem.</i> , 161 , 357, 1945.	
		ELLINGER and ABD EL KADER, <i>Biochem. J.</i> , 44 , 77, 1949.	
		SPECTOR et al., <i>J. biol. Chem.</i> , 161 , 145, 1945; WRIGHT and WRIGHT, <i>Proc. Soc. exp. Biol. Med.</i> , 49 , 80, 1942.	

Normal values in **grams** (unless otherwise stated) in **24-hour urine** on a normal balanced diet

	Normal values	Method and bibliography	Remarks
Blood	0	CAPLAN and DISCOMBE, <i>Brit. med. J.</i> , 2 , 774, 1951.	<i>Haematuria</i> occurs in glomerulonephritis, in renal infarction; in cases of tumours and tuberculosis of kidneys and bladder and of calculus in renal pelvis and bladder; in severe pyelitis and cystitis; in poisoning; in parasitic infestation (bilharziasis, filariasis).
Haemoglobin	0	spectrometrically (as oxyhaemoglobin)	In most pathological conditions the haemoglobin remains enclosed in the erythrocytes and <i>haemoglobinuria</i> is rare. Occurs particularly after blood transfusions with incompatible blood, in black-water fever; <i>paroxysmal nocturnal haemoglobinuria</i> (MARCHIAFAVA-MICHELÌ syndrome). “False” <i>haemoglobinuria</i> is due to haemolysis of erythrocytes in the bladder or <i>in vitro</i> . The renal threshold for haemoglobin in blood is ca. 150 mg/100 ml.
Methaemoglobin ...	0	spectrometrically	<i>Methaemoglobinuria</i> occurs in the same cases as haemoglobinuria, also in severe toxic and septic conditions, particularly after phenylhydrazine poisoning.
Myohaemoglobin ..	0	spectrometrically	<i>Myohaemoglobinuria</i> occurs in cases of severe destruction of muscle as a result of mechanical or electrical injury. Frequently not recognized as such but confused with haemoglobinuria.
Porphyrins			
Coproporphyrin I .	0.0147–0.080 mg	SCHWARTZ, S., <i>J. Lab. clin. Med.</i> , 37 , 843, 1951.	The method of determination given for coproporphyrin is very simple. The following procedure should be adopted: coproporphyrin is excreted mainly as colourless chromogen, the colour developing on standing under the effect of light. Fresh urine not exposed to light therefore usually gives lower coproporphyrin values. For this
Coproporphyrin III	0.0014–0.0343 mg		
Uroporphyrin I ...	}	GROTEPASS, W., <i>Hoppe-Seyler's Z. physiol. Chem.</i> , 253 , 276, 1938.	
Uroporphyrin III .			

reason the urine should be allowed to stand under light for 24 hours before the determination, care being taken that the reaction is neutral or alkaline. Acid urine should be neutralized as otherwise the acid-sensitive coproporphyrin will be decomposed during standing (cf. WATSON, C. J., *J. Lab. clin. Med.*, **37**, 831, 1951, and SCHWARTZ, S., *loc. cit.*).

The coproporphyrin excretion is increased (over 0.1 mg/day) in cirrhosis of the liver (in 94% of cases), in poisoning (lead, alcohol), in pernicious anaemia, in poliomyelitis. The excreted coproporphyrin originates from various organs, according to the nature of the disease: from bone marrow (lead poisoning, pernicious anaemia), from the liver (alcohol poisoning, cirrhosis of the liver) or from the nerves (poliomyelitis). In *uraemia* the coproporphyrin values are low (under 0.01 mg/day). Coproporphyrin excretion is an excellent criterion of liver function, with a sensitivity about equal to that of the bromsulphalein test (but not absolutely correlated with it) and greater than that of HANGER's test or the thymol turbidity test. Although the coproporphyrin excretion is not absolutely correlated with the clinical picture, the excretion as a rule increases with the extent of the damage to the liver. Patients with severe liver disease with foetor hepaticus, haemorrhagic oesophageal varices or incipient psychic disturbance always have high coproporphyrin values in urine. There is no correlation with either the directly or indirectly reacting serum bilirubin. Isomer III is generally higher in alcoholics, isomer I in non-alcoholics. In acute alcohol poisoning the coproporphyrin excretion increases for 2–4 days after the intoxication without other liver symptoms, and falls again during abstinence (cf. WATSON et al., *J. Lab. clin. Med.*, **37**, 8, 1951, and SUTHERLAND and WATSON, *ibid.*, **37**, 29, 1951).

Bilirubin	0	VAN DEN BERGH's test ..	The direct bilirubin is excreted <i>only</i> in the various forms of jaundice; the indirect bilirubin is never excreted. The renal threshold in adults amounts to 3–6 mg/100 ml, in children ca. 18 mg, in children with icterus gravis ca. 8 mg ¹ .
Urobilinogen	0.2–3 mg (1) 3–25 mg (2)	(1) by the method of WATSON, C. J., <i>Amer. J. clin. Path.</i> , 6 , 458, 1936; <i>Arch. intern. Med.</i> , 59 , 196, 1937. (2) by the method of SPARKMAN, R., <i>Arch. intern. Med.</i> , 63 , 858, 1939.	The colourless urobilinogen is the precursor of urobilin, into which it is converted on standing in air.
Urobilin	10–130 mg	BRADLEY, S. E., <i>Med. Clin. N. Amer.</i> , 29 , 1314, 1945.	Increases in hepatic disease, particularly in cirrhosis, congested liver, cholelithiasis, some forms of jaundice; in resorption of haemorrhages; very common in pernicious anaemia.
Melanogen	0	THORMÄHLEN's nitroprusside test.	Melanogen is colourless and is oxidized in air to the blackish melanin (in ca. 24 hours). THORMÄHLEN's test is specific for melanogen and is negative in alkaptonuria. Occurs in advanced disease due to melanotic tumours, mainly in their hepatic metastasis.

Colour of urine

Yellow or golden yellow	Normal
Light yellow, almost colourless, straw colour	Excessive liquid intake; reduced sweating; chronic interstitial nephritis; untreated diabetes mellitus; diabetes insipidus; alcohol; diuretics; nervousness.
Orange-yellow	Concentrated urine (after extreme sweating, in thirsting); fever; urobilin and other bile pigments; pyramidone and related drugs.
Orange to reddish brown	Drugs (senna, rhubarb).
Dark brown	Haemoglobinuria; phenolic drugs (phenol, cresol, phenylhydrazine); porphyrinuria.
Red	Blood; pyramidone, prontosil, aniline dyes (sweets); beetroot (anthocyaninuria).
Purple	Phenol red and phenolphthalein in alkaline urine.
Brownish wine-red ...	Porphyrinuria; mixture of met- and oxy-haemoglobin.
Brown to black	Haemoglobinuria; in phenol and cresol poisoning; melanin; alkaptonuria.
Greenish	Biliverdin; methylene blue; indigo carmine; after phenol, guaiacol, santonin.
Blue	Methylene blue, indigotin.

Turbidity

On standing, normal acid urine becomes slightly turbid (*nubecula*). Turbidity of alkaline urine is due to alkaline-earth phosphates (see under "Hydrogen-ion concentration", "Phosphates" and "Urinary sediments").

For turbidity due to fats and similar substances, see under Lipids, page 289.

¹) LARSEN and WITH, *Acta paediat. (Uppsala)*, **31**, Fasc. 1, 170, 1943.

Macroscopic examination: *Uric acid* and *urates* dissolve on warming to about 60°C and on addition of alkalis. *Phosphates* dissolve on addition of acetic acid, *oxalates* on addition of hydrochloric acid (for further differentiation see below). *Pus cells* clump together on warming, especially after addition of a little alkali.

Microscopic examination: The urine is allowed to stand in a sedimentation glass and the sediment layer then withdrawn by a pipette and centrifuged for 5 minutes. Where there is suspicion of kidney disease clear urine should also be centrifuged, since casts and other organized elements can be present.

Urinary sediments may be classified as follows:

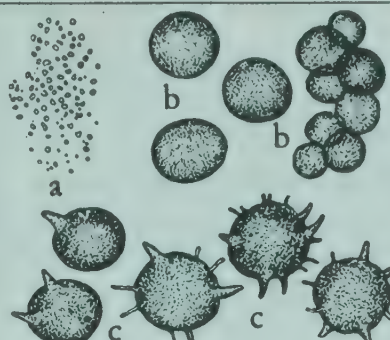
- 1. **Organized elements** (erythrocytes, leucocytes, epithelial cells, bacteria).
- 2. **Casts** from the uriniferous tubules (hyaline, granular, waxy, epithelial, erythrocyte, haemoglobin, leucocyte, cylindroid casts).
- 3. **Amorphous and crystalline chemical sediments** (see below and the opposite page).
- 4. **Miscellaneous** (mucus, spermatozoa, parasites [*Schistosoma haematobium* or *japonicum*, filaria, echinococci], foreign bodies [starch granules from face powder, mostly in urine of infants and women; hairs, textile fibres], oily substances [catheter lubricants]).

Amorphous and crystalline chemical sediments

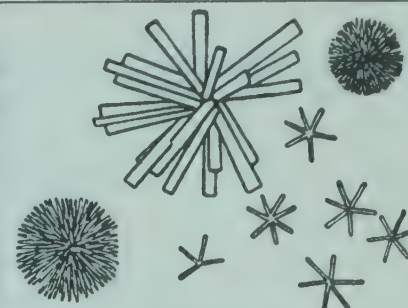
Sediment	Remarks	Occurrence		Solubility (○ = readily soluble, ● = sparingly soluble)						
		Alkaline urine	Acid urine	Heating	Alkalis	Mineral acids	Acetic acid	Alcohol	Acetone	Ether
Uric acid	Crystals mostly, but not always, coloured yellow by absorption of urinary pigments. Colourless usually smaller than coloured crystals.	acid	○ (60° C)	○	●	●	●	●	●
Urates	Calcium, magnesium and potassium urates, mostly amorphous, in concentrated acid urine. Colour and chemical behaviour as for uric acid.	Ammonium urate in alkaline urines	All other urates in acid urines	○ (60° C)	○	●	●	●	●	●
Phosphates star-shaped calcium phos- phate crystals ...	rare	alkaline	●	●	○	○	●	●	●
ammonium magnesium phosphate	commoner	alkaline	●	●	○	○	●	●	●
Calcium oxalate ...	Size about that of erythrocytes	See under acid urine	Usually in acid urine, also in neutral and weakly alkaline	●	●	○	●	●	●	●
Cystine	Colourless crystals (distinction from uric acid crystals, when of similar form). Must be looked for in fresh urine since rapidly destroyed by bacteria.	acid	●	○ esp. ammonia	○	●	●	●	●
Tyrosine	Often yellow-coloured since associated with jaundice. Mostly accompanied by leucine. In acute yellow atrophy of the liver, also in cirrhosis, acute phosphorus poisoning, leukaemia.	acid	● relative	○ precipitated on neutralization	○	○	●	●	●
Leucine	See tyrosine. Crystals in urine are impure. Pure leucine crystallizes in hexagonal platelets.	acid	○ relative	○	○	○	●	●	●
Bilirubin	Colours any uric acid crystals present and changes their shape.	acid	●	○	○	○	slight	○	slight
Indigotin	Rare. Also colours other crystals and thus appears to crystallize in various forms. Pure indigo in urine is amorphous or as (b) in figure opposite. From chloroform as (c) in figure.	alkaline	or acid	very soluble in chloroform				slight	—	○
Cholesterol	very rare	acid	very soluble in chloroform				slight	—	○
Hippuric acid	very rare	○	○	●	●	●	—	●
Sulphonamides ...	Easily distinguished from uric acid crystals by solubility in acetone.	—	—	—	—	—	○	—

Amorphous and crystalline chemical sediments¹

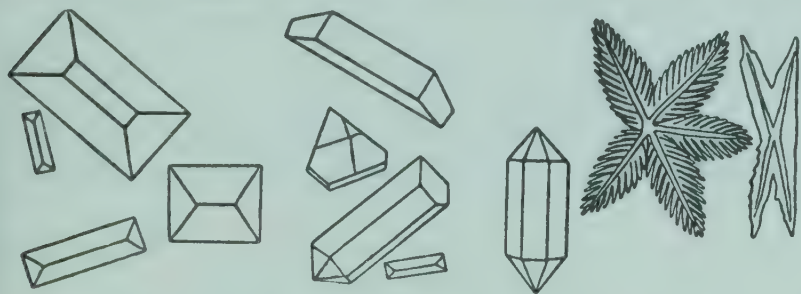
Various crystal forms of uric acid



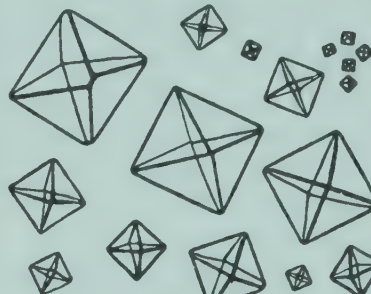
Urates



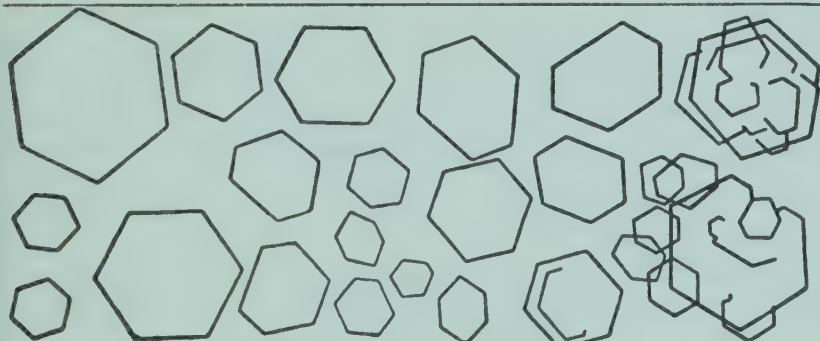
Star-shaped calcium phosphate crystals



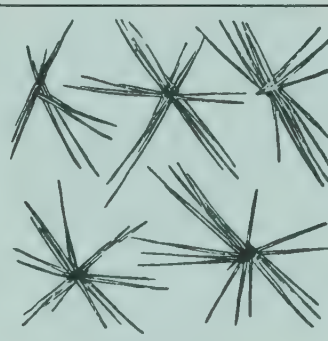
Ammonium magnesium phosphate crystals



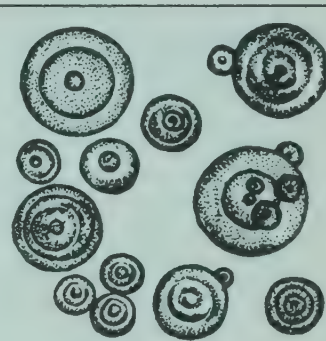
Calcium oxalate crystals



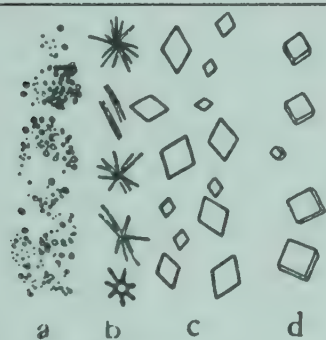
Hexagonal cystine crystals



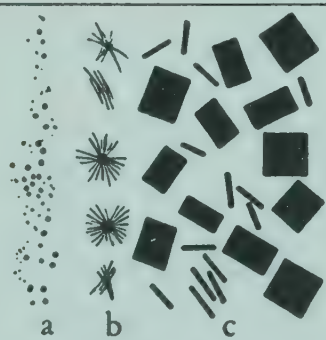
Tyrosine



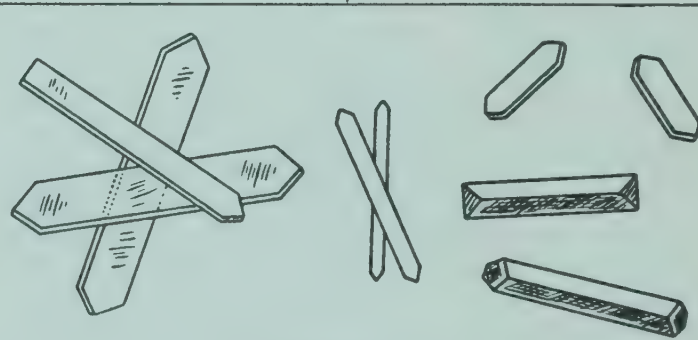
Leucine



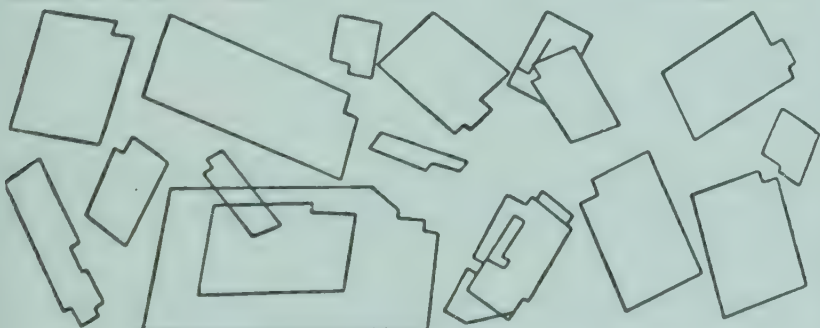
Bilirubin



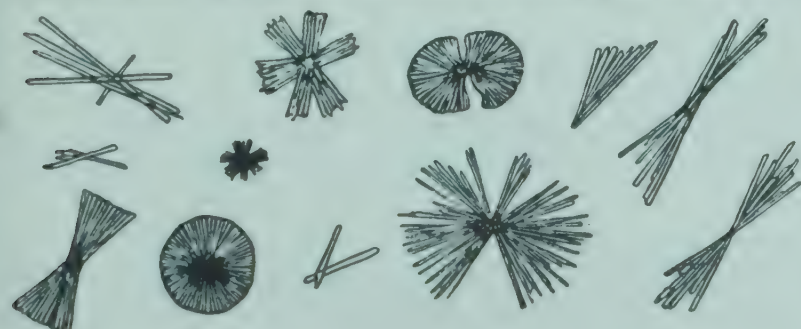
Indigotin



Hippuric acid



Jagged cholesterol platelets



Various sulphonamide crystals

Urates

- (a) calcium, magnesium and potassium urates, mostly amorphous
- (b) ammonium urate (spherical forms)
- (c) sodium urate (thorn-apple forms)

Calcium oxalate

- (a) octahedra, often flattened, the commonest form
- (b) dumbbell forms
- (c) ring forms

Bilirubin

reddish brown

- (a) amorphous
- (b) masses of needles
- (c) rhombic forms
- (d) cubic forms

Indigotin

blue

- (a) amorphous
- (b) masses of needles
- (c) rectangular platelets from chloroform

} urine

¹) After HARRISON, G. A., *Chemical Methods in Clinical Medicine*, London, 1947.

Only tests requiring a minimum of laboratory equipment are described

Proteins

**Acetic acid test:
(heat test)**

5 ml of clear urine, filtered if necessary, are heated to boiling for ca. $\frac{1}{2}$ minute with 0.5 ml SÖRENSEN's acetate buffer solution. SÖRENSEN's acetate buffer: solution of 56.5 g glacial acetic acid and 118.0 g sodium acetate cryst. in 1000 g distilled water.

Interpretation: When the urine contains more than traces of protein a fine flocculation appears. With a protein content of less than 1‰ an opalescent turbulence first appears, developing into a similar fine flocculation after several minutes standing or on further boiling.

Alkaline-earth phosphates or urates give no precipitate in this test, which is also independent of the pH value of the urine.

**Sulphosalicylic acid
test:**

(Very sensitive test for very small protein concentrations.) 5 ml of clear, slightly acid urine, filtered if necessary, are added dropwise to 0.5 ml 25% sulphosalicylic acid solution.

Interpretation: In the presence of proteins a white turbulence is formed, not cleared on warming. If it is difficult to decide whether turbulence has formed or not, compare the treated sample against the light with an untreated one. The test is positive for protein concentrations of 0.015‰ upwards. If the urine is somewhat alkaline, rather more sulphosalicylic acid must be added.

In certain circumstances (rare) uric acid can simulate a positive reaction, but in this case the turbidity, in contrast to that due to proteins, disappears on warming.

Sugar

FEHLING's test:

5 ml of urine in one test tube and 5 ml of a mixture of equal parts of FEHLING's solutions I and II in another test tube are heated almost to boiling (avoid boiling) over the same flame, and the FEHLING's solution then poured slowly into the urine. Very concentrated urine should be diluted beforehand. FEHLING's solution I: solution of 3.5 g copper sulphate in 50 ml dist. water. FEHLING's solution II: solution of 17.5 g potassium sodium tartrate (Rochelle salt) and 5 g sodium hydroxide in 50 ml dist. water.

Interpretation: In the presence of sugar a more or less abundant precipitate of yellowish-red cuprous oxide, according to the amount of reducing substances present, is formed. On further heating the mixture a greenish precipitate sometimes appears, indicating the presence in the urine of substances with a strong alkaline action.

BENEDICT's test:

5 ml of BENEDICT's reagent are mixed with 0.5 ml urine and the mixture boiled vigorously for 2 minutes.

BENEDICT's reagent: 173 g sodium citrate, 100 g anhyd. sodium carbonate, 17.3 g cryst. copper sulphate. The sodium citrate and carbonate are dissolved in ca. 600 ml dist. water and the copper sulphate in a separate receptacle in ca. 100 ml dist. water. The latter solution is then added with constant stirring to the former, the mixture filtered if not clear, and made up to 1000 ml with dist. water. The reagent may be stored indefinitely.

Interpretation: In the presence of sugar a yellowish or reddish precipitate is formed. In certain circumstances (rare) alkaline-earth phosphates can simulate a positive reaction by giving a whitish or greyish precipitate.

Acetone bodies

ROTHERA's test:

(modification of LEGAL's test):

10 ml of urine are mixed with ca. 2 ml of concentrated ammonia and ca. 2 g of a dry powdered mixture of 100 parts ammonium sulphate and 1 part sodium nitroprusside and the test tube stoppered, shaken vigorously and allowed to stand.

Interpretation: In the presence of acetone, acetoacetic acid or both, a characteristic purple coloration (resembling permanganate) is developed, the intensity of which is proportional to the concentration of acetone bodies. The test is more sensitive to acetoacetic acid than to acetone.

GERHARDT's test:

for acetoacetic acid:

The test must be made with the freshest possible urine since acetoacetic acid is readily decomposed into CO₂ and acetone. – 5 ml of urine are mixed with ca. 2–3 ml of a 10% ferric chloride solution.

Interpretation: In the presence of acetoacetic acid the mixture turns a wine-red colour. This coloration is also produced by salicylic acid or drugs such as aspirin but since these substances, in contrast to acetoacetic acid, are not destroyed by boiling, their presence may be detected by repeating the test using boiled urine. If the result of this second test is negative then the coloration in the first test can be ascribed to acetoacetic acid.

By A. F. ESSELLIER and P. JEANNERET, University Medical Clinic, Zurich (Prof. W. LÖFFLER)

The scope and content of this section have been decided by practical considerations. It is not intended as a full treatment of the subject but as a summary of data in frequent use which would otherwise have to be individually collated from the various special fields concerned, such as Blood, Urine, Renal function, etc. In consideration of the general scope and purpose of these *Scientific Tables* a number of definitions and explanations have also been included. In general, however, it has been assumed that the reader is familiar with the present state of knowledge in the field of water and electrolyte balance.

An important complement to this section is provided by the text and tables in the section "Aqueous Solutions" on pages 114-125. There the reader will find definitions and conversion factors for "mole" and "gram equivalent", chemical units of measurement which are indispensable in this field, together with a summary and detailed description of parenteral infusion solutions for fluid and electrolyte replacement therapy.

Functionally, water balance and electrolyte balance are inseparable since the chemically uncombined water of the body forms practically an isotonic solution with a relatively constant electrolyte content and a somewhat less constant content of organic substances. Changes in any one component therefore inevitably bring about changes in the others. This functional dependence should be kept in mind when making use of the data given in this section of the *Tables*, where a general discussion of body water will be followed by consideration of its electrolytic constitution.

I. Water balance

A. Distribution of water

The distribution of water between the various parts of the body (intra- and extra-cellular water, etc.) permits a calculation of the respective contents of dissolved minerals. Sodium and chloride ions are found mainly in the extracellular fluid and must be related to this latter in calculations. A deficiency of these ions is therefore indicated by their serum level. Potassium ions, on the other hand, are concentrated mainly intracellularly and the extent of a deficiency cannot simply be deduced from the serum level. Potassium deficiency is indicated by clinical symptoms but can only be accurately estimated by balance methods.

Total body water	Percentage of body weight	
	Mean	Range
Average values for adults		
Deuterium oxide method ¹⁴	%	%
Men, 17-34 years	61.1	53.3-70.3
57-86 years	54.3	47.8-62.8
Women, 20-31 years	51.2	45.6-59.9
60-82 years	46.2	42.0-53.4
Antipyrin method ⁴⁶		
Men	53.6	-
Women	46.2	-

The more accurate deuterium oxide method gives higher values than the simpler antipyrin method, particularly with oedematous patients²⁵.

The percentage water content is more closely related to the body surface area than to the body weight^{39a} and varies in inverse proportion to the fat content of the body^{14, 61}; the latter circumstance explains the general difference in water content between men and women. The percentage water content diminishes with increasing age⁶¹. In infants* it is considerably higher than in adults²⁰.

Extracellular water	Percentage of body weight	
	Mean	Range
Average values for adults		
a) Total extracellular water (inc. plasma water)	%	%
Thiosulphate method (men) ⁸	16.6	-
Inulin method ²⁹	15	-

The volume of thiosulphate or inulin distributed is not extended to the "trans-cellular" water¹⁶, i.e. to the cerebrospinal fluid, glandular or intestinal cavities, renal pelvis, etc.

b) Plasma volume		
EVANS Blue method after GIBSON ²²		
Men	4.3	3.2-5.8
Women	4.1	3.3-5.2
For other methods, see page 305.		

Conversion of plasma volume to plasma water^{39a}

Plasma water in millilitres =

Plasma vol. (ml) × (98.40-0.718 × protein content in g/100 ml serum) / 100

c) 'Interstitial water'

Obtained as the difference between total extracellular water and plasma water.

Intracellular water

Obtained as the difference between total body water and extracellular water.

Average value for adults (antipyrin distribution volume minus inulin distribution volume)⁶: 40% of body weight.

The distribution of water in the various parts of the body, like the total water content, is more closely related to the body surface area than to the body weight^{39a}.

None of the methods described above is generally applicable to clinical purposes. The state of hydration must usually be judged by other criteria, such as elasticity of the skin and of the subcutaneous tissue, blood pressure, specific gravity of urine, etc. Since the relative volume of the intracellular water is a function of the effective osmotic pressure of the extracellular water the elasticity of the skin and of the subcutaneous tissue indicates primarily not the actual level of the intracellular water but that of the extracellular water.

The distribution between intra- and extra-cellular water may be estimated from the sodium content of the serum, the plasma volume from the haematocrit value, the erythrocyte count or the haemoglobin content. Although diminution of the extracellular water and of the blood concentration often run parallel, exceptions to this are so frequent that only after a careful assessment of the whole clinical picture may reliable conclusions be drawn.

In the case of rapid changes in the state of hydration valuable conclusions may be drawn from comparisons between body weight and erythrocyte count or protein content.

The following may be regarded as clinical norms for water content and distribution:

	Men	Women	
Total water	60 %	55 %	} of body weight
Extracellular water	15 %	15 %	
Intracellular water	45 %	40 %	

B. Daily intake and elimination of water

The water intake is made up of the water content of the liquid and solid nutriment together with the "water of oxidation" arising from intermediate metabolism. 100 g of fat yield ca. 100 ml, 100 g of protein ca. 40 ml and 100 g carbohydrate ca. 60 ml of water of oxidation. For a simplified clinical water balance the water of oxidation may be regarded as equal to the water of the faeces, provided that there is no diarrhoea. For patients in bed on a normal diet, without fever or sweating, the water content of the solid food is sufficient to meet the extrarenal water loss via the skin and lungs (= invisible transpiration).

The following may be regarded as clinical norms (rest, moderate climate, no fever, no visible transpiration):

Water intake, total	2500 ml
as liquid	1500 ml
with food (including 300 ml water of oxidation)	1000 ml

Under normal conditions the water intake is adjusted by thirst to meet very closely the actual water requirements of the body. The sensation of thirst is actuated and controlled by various factors such as the water content of the cells (in turn dependent on the electrolyte concentration of the extracellular water), the plasma volume (maintenance of the blood circulation), etc.

Water elimination

The water elimination is made up of the losses via the skin and lungs (= invisible transpiration), the faeces and the urine.

The following may be regarded as clinical norms (rest, moderate climate, no fever, no visible transpiration):

Water elimination, total	2500 ml	(c) via the skin and	
(a) via the skin	500 ml	lungs	900 ml
(b) via the lungs	400 ml	(d) faeces	100 ml
		(e) urine	1500 ml

* For children up to 20 kg, total water content²⁰ (in litres) = (0.55 × body weight in kilograms) + 0.51.

I. Water balance (continued)

- (a) *Water elimination via the skin*
Rest, moderate climate, no fever, no visible transpiration^{37, 42, 59} 400– 600 ml
Under tropical working conditions (DILL, quoted in ²¹) 8000–10,000 ml
Rest, moderate climate, body exposed to the sun (DILL, quoted in ²¹) 400 ml
- (b) *Water elimination via the lungs*
Rest, moderate climate^{34, 42} 400 ml
- (c) *Water elimination via the skin and lungs (invisible transpiration)*
Rest in bed, no fever, no visible transpiration^{42, 47} 800– 1000 ml
Rest in bed, fever, mild sweating⁴⁷ 1500 ml
Rest in bed, fever, profuse sweating⁴⁷ 2000 ml

The loss of heat by evaporation amounts to ca. 24% of the total loss of heat (after SODERSTROM and DUBOIS in ³⁹). Taking into consideration the heat of vaporization of water at 37° C (0.58 kcal/ml) the extrarenal water loss, except in excessive sweating, can be calculated from the calorie consumption by means of the following formula:

Water loss by evaporation (in ml)
= 0.414 × calorie consumption (after NEWBURGH in ³⁹).

Thus with a calorie consumption of 2000 kcal, for example, a water loss via the skin and lungs of ca. 825 ml is to be expected. The calorie consumption must not be assumed to be the same as the calorie intake. In fever, for example, the calorie consumption (heat production) is usually greater than the calorie intake.

- (d) *Water elimination via the intestinal tract*
Faeces: the normal water content amounts to ca. 70–80%, or 4 ml water per 100 calories food intake¹². The total quantity per day^{12, 60} amounts to 160–250 g on a mixed diet, up to 370 g on a vegetable diet, only 54–64 g on a meat diet.

Intestinal water circulation^{36, 57} (loss only by surgical drainage):

	Mean (ml)	Range (ml)
Saliva	1500	500– 1500
Gastric juice	2500	1000– 5000
Bile	500	100– 1000
Pancreatic juice	700	700– 1000
Intestinal juice	3000	700– 3000
Total	8200	3000–11,500

- (e) *Water elimination by the kidneys*⁵⁷: 600*–1600 ml. Cf. page 299.

Water loss by evaporation in warm weather and that due to the water requirement of a deficient kidney (lowered concentration capacity) are often underestimated.

II. Osmotic relations of the body fluids

The osmotic relations are of importance with regard to the distribution of water between the extra- and intra-cellular spaces,

between the vascular and perivascular spaces, and for the filtration processes of the body.

The water equilibrium between the *intracellular* and the *interstitial* space depends on the reciprocal concentrations of osmotically active particles (molecules and ions).

The distribution of water between the *vascular* and the *interstitial* space depends on the following factors^{39a}:

Lymph drainage	
(a) {	(b) {
Capillary pressure	Tissue tension
Oncotic pressure of the interstitial fluid	Oncotic pressure of the plasma

where the factors (a) favour transudation from the capillaries and the factors (b) retard this transudation. The interstitial fluid is an ultrafiltrate of the plasma and differs from this latter only in its much lower protein concentration.

Osmotic pressure of plasma at 38° C:
7.70 atm or 5852 mm Hg.

This osmotic pressure corresponds to a **freezing-point depression** of 0.56° C or an **osmolality** (concentration of all osmotically active particles) of 301.4 mosm (mmol).

Oncotic pressure (colloid-osmotic pressure) of serum:
30–40 cm water = 0.03–0.04 atm = 23–30 mm Hg.

Capillary pressure (after LANDIS, quoted in ⁶²):
average 32 mm Hg = 43.4 cm water at the start of the femoral artery;
12 mm Hg = 16.3 cm water at the end of the femoral vein.

In the case of an abnormal combination of plasma proteins the *oncotic pressure* can be calculated from KEYS' formula (quoted in ⁶¹):

Oncotic pressure (in mm water) = $f_c (45.2 A + 18.86 G) \times T/273.16$,
where A = albumins in g/100 ml serum, G = globulins in g/100 ml serum, T = absolute temperature in °K = 273.16 + °C, and f_c is a factor which varies with the total protein content in the following way:

Total protein content of serum								
in g/100 ml:	1	2	3	4	5	6	7	8
f_c :	0.88	0.92	0.98	1.03	1.09	1.17	1.28	1.45

Since fibrinogen on account of its high molecular weight exerts practically no osmotic pressure the oncotic pressures of the serum and the plasma can be considered as equal.

For conversion of freezing-point depression into osmotic concentration and osmotic pressure and vice versa, see page 117. For conversion of pressure units, see pages 60 and 61.

The osmotic concentration (ideal osmolality) calculated from the chemical composition on the assumption of *complete dissociation* of the strong electrolytes (mineral salts, mainly NaCl) amounts to ca. 325 mmol per 1000 g serum water (see figure 1). The difference between this value and the *actual effective* osmotic concentration of ca. 300 mosm (mmol) per 1000 g serum water (real osmolality) is accounted for by the fact that the actual dissociation of the electrolytes is somewhat less in serum.

* Normal minimal elimination.

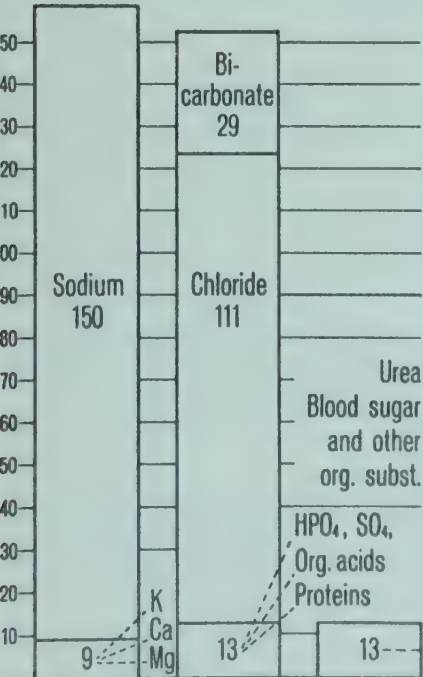


Fig. 1. Concentration of the osmotically active components of serum in mmol/l (or mmol/1000 g) serum water, calculated from the analytical values of JEANNERET et al.²⁷ on the assumption of complete dissociation. – Fig. 2. Ionogram after GAMBLE²¹, modified. Cf. the following page. The weakly dissociated carbonic acid (H₂CO₃) has been disregarded. More recent

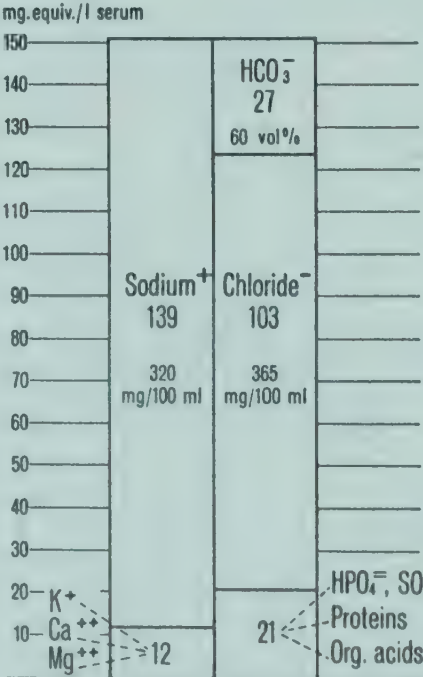


Fig. 2

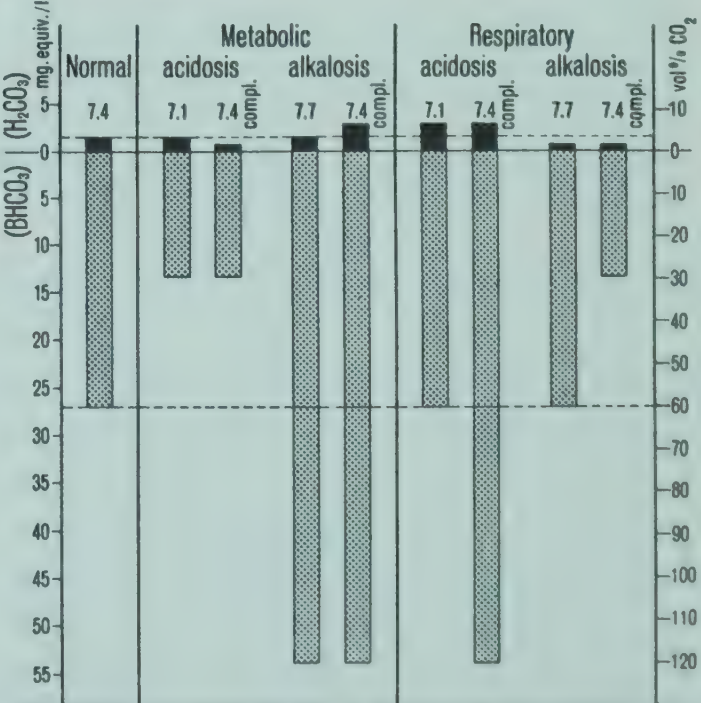


Fig. 3

data give a sodium content of 139 mg. equiv./l serum and a total acid or base content of 151 mg. equiv./l in place of GAMBLE's values of 142 and 155 mg. equiv./l respectively²¹. – Fig. 3. Relations between carbonic acid (H₂CO₃), bicarbonates (BHCO₃) and the pH of the blood in acidosis and alkalosis. Cf. the following page and page 330. After GAMBLE²¹.

III. Serum levels of the clinically most important electrolytes

Acid-base relationships and calculations involving them are based on the chemical mass unit "gram equivalent" (equiv)*, corresponding to a quantity of ions with a total of 6.023×10^{23} (free) electrical valencies. One gram equivalent of any one kind of ion therefore contains the same number of valencies as any other kind of ion, whereby the absolute weights as well as the molecular weights of the two kinds of ions may be quite different. The gram equivalent is calculated from the mole by means of the valency of the ions concerned (cf. pages 114 and 115, and the conversion tables for electrolytes on pages 118–120). For univalent ions (Na^+ , K^+ , Cl^- , HCO_3^- , etc.) it is identical with the mole. Conversion factors for concentrations in mg/100 ml (or g/100 ml or vol%) and mg. equiv/l are given in the right-hand columns of the table below.

When the concentrations of the serum electrolytes are expressed in milligram equivalents per litre they can be represented in the now usual form of an ionogram (first due to GAMBLE²¹, see fig. 2), in which the sums of the cations and of the anions are represented by columns. Since in serum, as in all other electrolytic solutions, the positive and negative valencies are in equilibrium (electrical neutrality) the columns are of equal height. When changes in the ionic constitution of one column occur, or when there is a change in the total cation or anion content, the heights of the two columns remain the same. A rise or fall in the chloride level, for example, is balanced by a corresponding opposite movement in the bicarbonate level, changes in the sodium content result in corresponding changes in the sum of the anions, and so on.

Changes of this sort are always accompanied by changes in the pH value. The serum has a buffering action, however, and the physiological pH limits (see page 308) are only exceeded when this buffering capacity is exceeded. An acidosis or alkalosis is thus respectively referred to as *compensated* or *uncompensated*. Quantitatively, by far the most important buffer system of the blood consists of the system carbonic acid (H_2CO_3)/bicarbonate (BHCO_3), where B = a univalent cation, nearly always Na^+ . Its function is shown by the HENDERSON or HENDERSON-HASSELBALCH equation (see page 330).

A measure of the bicarbonate content (denominator in the HENDERSON equation) which is usually adequate for clinical purposes is provided by the so-called **alkali reserve** of serum (CO_2 combining capacity, etc.; for definition and determination, see page 330). This can be expressed either as bicarbonate- CO_2 in vol% or as bicarbonate ions (HCO_3^-) in mg. equiv. A decreasing alkali reserve usually indicates a tendency to acidosis, an increasing one a tendency to alkalosis. A reliable diagnosis, however, must unquestionably be based on the whole clinical picture (e.g. KUSSMAUL's respiration in acidosis, tetany in alkalosis; also increased urinal elimination of ammonia and acids in acidosis, of bicarbonate in alkalosis, given an intact renal function, etc.). An unequivocal criterion of changes in alkali reserve is provided by the pH of the blood (see fig. 3), in accordance with the following relation:

Increase of the alkali reserve over ca. 60 vol% indicates an acidosis if the pH is less than 7.4 and an alkalosis if the pH is greater than 7.4; decrease of the alkali reserve under ca. 60 vol% indicates an alkalosis if the pH is greater than 7.4 and an acidosis if the pH is less than 7.4.

(Primary) **metabolic acidosis** arises as a result of the *accumulation of large quantities of acids* stronger than H_2CO_3 , through increased acid production (in hunger, extreme physical exertion, diabetes mellitus, etc.), through exogenous administration of acids (e.g. ammonium chloride) and through acid retention (kidney disease), or as a result of *severe loss of bases* (diarrhoea, intestinal or biliary drainage or fistulas, ADDISON's disease). (Primary) **metabolic alkalosis** arises as a result of *severe loss of acids* (vomiting, gastric drainage, etc.) or as a result of *inadequate intake of alkalinizing salts* (sodium bicarbonate, lactate, etc.).

(Primary) **respiratory acidosis** occurs when the *expiration of CO_2 is impeded* (stenoses of the upper respiratory passages, hypopnoea of central origin, pulmonary emphysema, etc.), (primary) **respiratory alkalosis** in *hyperventilation* (e.g. salicylate poisoning). The determination of the alkali reserve is not sufficient for estimating changes in acid-base relationships of respiratory origin. For this purpose the actual bicarbonate- CO_2 content must be measured (cf. page 330, normal values page 331).

The serum values which are most important in electrolyte balance have been summarized below and include the data of various workers. Values differ from author to author, partly as a result of differences in the method of determination. Flame-photographic methods in general give somewhat higher values. Although lying inside the limits of physiological variation the serum value for Na (142 mg. equiv/l) and the total height of the column (155 mg. equiv/l) in GAMBLE's ionogram²¹ are probably somewhat too high.

The following electrolytes must be added to those listed in the table: Mg^{++} (1.7 mg. equiv/l), sulphates as SO_4^{--} (0.7 mg. equiv/l)², anions of organic acids, complex electrolytes of proteins and lipids. Since the anions of the organic acids, the proteins and the lipids are extremely difficult to determine analytically and can only be approximately calculated (proteins, see footnote****) there is always a factor of uncertainty in building up the anion column. In practice therefore, since the anion and cation columns must be of equal height, the height of the ionogram is based on the sum of the cations, which can be determined analytically with accuracy (fig. 2, left-hand column). The anion concentrations are then marked off on the right-hand column, starting at the top with HCO_3^- and Cl^- , followed by HPO_4^{--} and SO_4^{--} if they have been separately determined. The remaining length of the column at the bottom then corresponds to the proteins and undetermined acids ("residual acids"). The total cation (or anion) equivalent is given by GAMBLE²¹ as 155 mg. equiv/l, by PETERS^{39a} as 149 mg. equiv/l. SHOHL⁴⁸ gives analytical values for total cation and anion equivalents of 155.2 and 150 mg. equiv/l respectively.

Serum levels of the clinically most important electrolytes		Normal values					Conversion factors	
		GAMBLE ²¹		JEANNERET, ROSENMUND, ESSELLIER ²⁷		PETERS ^{39a}	mg/100 ml or g/100 ml or vol% into mg. equiv/l Serum	mg. equiv/l into mg/100 ml or g/100 ml or vol% Serum
		Mean values		Mean		Mean and range		
Cations	Concentration	Serum	Serum water**	Serum		Serum		
Sodium	{ mg. equiv/l mg/100 ml	142 326.6	152.0 349.6	139.2 320	136.6 – 141.8 314 – 326	138.0 ± 3.4 317.5 ± 7.8	{ 0.435	2.30
Potassium	{ mg. equiv/l mg/100 ml	5 19.6	5.4 21.1	5.1 20	4.1 – 5.6 16 – 22	4.1 ± 0.3 16.0 ± 1.2	{ 0.256	3.91
Calcium	{ mg. equiv/l mg/100 ml	5 10	5.4 10.8	5.0 10	4.7 – 5.2 9.5 – 10.5	5.3 ± 0.3 10.6 ± 0.6	{ 0.499	2.00
Anions								
Chlorides	{ mg. equiv/l mg/100 ml	103 365.7	110.3 391.6	102.9 365	97.3 – 107.2 345 – 380	102.2 ± 2.2 362.8 ± 7.8	{ 0.282	3.55
Alkali reserve:								
Bicarbonate	mg. equiv/l	27	28.9	26.9	23.8 – 34.7	26.5 ± 1.4	{ 0.449 ***	2.23 ***
Bicarbonate- CO_2	vol%	60.2	64.5	60	53 – 77	59.1 ± 3.1	{	
Serum proteins	{ mg. equiv/l g/100 ml	16 6.6	17.1 7.5	16.9 7.0	15.7 – 18.1 6.5 – 7.5	17.3 (incl. organic acids)	{ 2.41 ****	0.41 ****
Phosphates (inorg.)	mg. equiv/l	2	2.1	1.7	1.5 – 2.0	2.0 ± 0.5	{ 0.581 †	1.72 †
Inorg. phosphorus	mg/100 ml	3.4	3.6	3	2.5 – 3.5	3.4 ± 0.86	{	

The mg/100 ml values of GAMBLE and of PETERS have been obtained by conversion of the authors' mg. equiv/l values using the factors given.

* The internationally recognized symbol is val.

** Calculated from the serum value using the formula^{39a}: serum water (in ml/100 ml serum) = 98.4 minus $0.718 \times$ protein content in g/100 ml serum, assuming an average protein content of 7.0 g.

*** In connection with conversion factors see footnote on page 120.

**** VAN SLYKE's factor⁴⁹ of 2.41 for conversion of serum protein content (g/100 ml) into ionized serum protein (mg. equiv/l) is valid for 38°C, pH 7.4 and an albumin/globulin ratio of 1.8. In the case of an abnormal distribution of protein fractions it should be possible according to VAN SLYKE to calculate the base equivalence of the albumins and globulins by means of the following factors: 1 g albumin-N = 1.745 mg. equiv, 1 g globulin-N = 1.205 mg. equiv. According to BROCH⁷, however, the base equivalence is greatly reduced in dysproteinemia so that in this case VAN SLYKE's conversion would give too high a value.

† At pH 7.4 and 38°C.

IV. Average sodium-, potassium- and chloride-ion contents of body fluids and secretions important to electrolyte balance

The following table summarizes data on the average sodium-, potassium- and chloride-ion contents of body fluids the loss of which can lead to an electrolyte deficiency (vomitus, watery stool, and drainage, enterostomy and puncture fluids, etc.). The corresponding urine values are given on the next page; in individual cases they can show very large variations. The sodium chloride contents of these fluids have not been given, since in most cases the ratio of Na to Cl is 1:1.

A rational electrolyte replacement therapy is particularly important in cases of disturbed renal function, when the tubular regulation of the water and mineral metabolism is affected

(postoperative conditions, etc.). In view of the practical difficulties of attaining even an approximate electrolyte balance the question may well be asked, why does a determination of the electrolyte values in serum not suffice for a correct, i.e. quantitatively adequate, replacement therapy? *Sodium* losses lead to a reduction in the extracellular fluid, so that the lowering of the sodium level in serum does not correspond to the actual sodium loss. For this reason a severe loss of body water can be accompanied, in spite of sodium deficiency, by an approximately normal serum sodium level. *Chlorine* loss, on the other hand, is indicated at once by the chloride-ion concentration in the serum, since chlorine loss alone does not result in any particular loss of extracellular fluid. *Potassium* deficit is reflected only at a late stage by the serum potassium level, since the serum potassium loss is for a long time compensated by release of cell potassium.

	Na ⁺		K ⁺		Cl ⁻	
	mg. equiv/l	mg/100 ml	mg. equiv/l	mg/100 ml	mg. equiv/l	mg/100 ml
1. Mean values in serum water, after GAMBLE (see page 297)	152	350	5.4	21	110	392
2. Serum ultrafiltrate	139	320	4.4	17	114.2	405
3. Transudates	144	331	4.9	19	112	397
4. Sweat ¹ , mean value	58.4	134	10.0	39	45.4	161
standard deviation σ	15.7	36	2.4	9	15.5	55
5. Saliva ⁵⁸ , mean value	33.1	76	19.5	76	33.9	120
standard deviation σ	13.4	31	3.4	13	10.2	36
6. Gastric juice, total ⁴² , mean value	59.0	136	9.3	36	89.0	316
² / ₃ of cases	31-90	71-107	4.3-12.0	17-47	52-124	184-440
from ¹¹	20-80	46-184	5-20	20-78	100-150	355-532
7. Gastric juice, fundus ⁴⁸	35	80	15	59	160	567
Gastric juice, pyloric ⁴⁸	160	368	25	98	140	496
8. Bile ⁴² , average	145.3	334	5.2	20	99.9	354
² / ₃ of cases	134-156	308-359	3.9-6.3	15-25	83-110	294-390
from ¹¹	120-140	276-322	5-15	20-59	80-120	284-425
9. Pancreatic juice ⁴²	141.1	324	4.6	18	76.6	272
from ¹¹	120-140	276-322	5-15	20-59	40-80	142-284
10. Intestinal juice ⁴² , MILLER-ABBOTT catheter						
average	104.9	240	5.1	20	98.9	350
² / ₃ of cases	72-128	166-296	3.5-6.8	14-27	69-127	245-451
from ¹¹	100-140	230-322	5-15	20-59	90-130	319-461
11. Ileal secretion ⁴² , MILLER-ABBOTT catheter						
from a fresh ileostomy, average	116.7	268	5.0	20	105.8	376
² / ₃ of cases	129.5	298	16.2	63	109.7	389
from ¹¹	112-142	258-326		18-55	93-122	330-433
12. Caecostomy secretion ⁴² , average	79.6	183	20.6	81	48.2	171
² / ₃ of cases	48-116	110-266	11.1-28.3	43-111	35-70	124-248
13. Formed stools (values relate to the water content) ³⁹						
Calculated average	35	81	72	282	73	259
Extreme values	7-96	16-221	34-150	133-587	17-164	60-582

Remarks

In view of the large variations in the composition of the fluids of the digestive tract, prior determination of the Na-, K- and Cl-ion contents is essential for an effective electrolyte replacement therapy.

Ad. 2. The values in serum ultrafiltrate have been calculated from the mean values in serum water by means of PETERS' ratios for serum water/serum ultrafiltrate (Na: 0.9, K: 0.82, Cl: 1.03)³⁹. The values in serum ultrafiltrate are largely in agreement with those for the nearly protein-free interstitial fluid.

Ad. 3. The ratios of the electrolytic contents serum water/transudate are 0.96 for Na, 0.92 for K, 1.03 for Cl^{18,39}. The values given above have been calculated from the mean values in serum water using these ratios, on the assumption of an average protein content in transudate of 2 g/100 ml.

Ad. 4. The values given are for sweat samples from the forearm obtained by means of artificial warmth. After adaptation to a hot climate the Na- and Cl-values are much lower¹⁰. According to AHLMAN et al.¹ the Na/Cl ratio (mg. equiv/l) amounts to 1.32 ± 0.15 , according to BERENSON and BIRCH⁴ 1.14 average. In contrast to saliva, there is no diagnostically significant Na/K ratio in sweat^{1,4}. During a sudation test the Na- and Cl-concentrations rise in the course of an hour to double the initial values⁴. The values given above¹ are the maximum values observed after one hour's sudation⁴.

Ad. 5. According to FRAWLEY and THORN¹⁹ the ratio of Na/K in saliva averages 1.3 ± 0.5 with a range of 0.33-2.1. This ratio rises in ADDISON's disease to 2.2 ± 0.5 . If the Na level in serum lies below 132 mg. equiv/l this characteristic increase of the Na/K ratio may not be observed⁵⁶. The values for this ratio¹⁹ and those given above for Na⁵⁸ were measured after normal alimentary salt intake and after stimulation of salivation by chewing of paraffin wax. Saliva obtained by simple aspiration, i.e. without stimulation, has a markedly lower Na content (mean value 8.3 mg. equiv/l, range 4.8 to 14.6 mg. equiv/l)⁵⁶.

Ad 6. The average fasting values given (after RANDALL⁴²) are based on 130 measurements on gastric juice ranging from anacidity to hyperacidity. The Na/Cl ratio in a hyperacid gastric juice can fall to ¹/₃ of the normal value. In an acidity the total gastric juice can contain as many chloride ions as sodium ions, not, however, in the form of HCl but as salts^{31,42}. A high sodium content can also be due to a reflux of duodenal juice. RANDALL's potassium value⁴² of 9.3 mg.equiv/l is low; according to MARTIN³⁶ the potassium concentration averages 16.5 mg.equiv/l, according to SAEMUNDSON⁴³ 17.1-21.8 mg. equiv/l, according to MACH³² 22-29 with mean 26 mg. equiv/l.

Ad 8 and 9. Values from RANDALL⁴² in surgical fistula fluids.

Ad 11. In ileostomy a lowering of the electrolyte content of the secretion eventually takes place³⁰.

Ad 12. The Na- and Cl-concentration in the caecostomy secretion is about half that in the ileostomy secretion³⁰.

Ad 13. The analytical values given relate to the water in the faeces (mg. equiv/l water). The normal electrolyte elimination can also be expressed as a percentage of the total excretion (faeces + urine); the values are then roughly 5% for Na, 21% for K, 2% for Cl⁴⁸.

In *diarrhoea* it is difficult to estimate the electrolyte loss via the faeces; the more watery the stool the more nearly the electrolyte concentration approaches that of the ileal secretion⁴⁸. According to BARTLETT et al. (quoted in ³⁹) the mean value for Cl is 73 mg. equiv/l (63-89 mg. equiv/l). The usually higher potassium loss in diarrhoea is of greater practical significance. In artificial diarrhoea provoked by anthraquinone laxatives⁴⁵ potassium concentrations in the stool of 50-55 mg.equiv/l have been observed, in cases of ulcerative colitis⁴¹ 38-43 mg. equiv/l. According to DARROW¹⁸ diarrhoea stools of infants contain ca. 64 mg.equiv/l Na, 44 mg.equiv/l Cl and 32 mg. equiv/l K, with faecal quantities of ca. 250 ml.

V. Renal function values

The table (a) contains a summary of average values in health for the filtration, reabsorption and elimination of important electrolytes. These values demonstrate the high filtration capacity of the kidneys for sodium and chloride, which are present in high concentration in serum, and the markedly smaller filtration capacity for potassium and phosphate, of which the serum levels are low. The figures, as well as the fact that 137 litres per day are filtered by the glomeruli, explain why the retention of sodium, chloride and water, so long as a diuresis persists, must be due to increased tubular reabsorption. The figures also show that if the glomerular filtration is reduced a retention* of phosphate must

soon occur, while no retention of sodium or chloride takes place. Under (b) the relations between specific gravity and osmotic concentration are briefly discussed. Under (c) the clinically important relations between specific gravity and diuresis in isosthenuria are described. Under (d) (on the next page) will be found normal values for various quantitative tests of renal function. This summary has been inspired by the fact that normal values are not usually to be found in the literature in connection with the results of renal function tests.

(a) Elimination of electrolytes

	Average concentration in 24-hour urine		Average elimination	Glomerular filtration of electrolytes	Tubular reabsorption of electrolytes
	mg. equiv/l	mg/100 ml	g/24 hours	g/24 hours	% of the quantity filtered
<i>Cations</i>					
Sodium	90	207	3.11	438	99.4
Potassium*	50	196	2.94	23.6	88
Calcium	5	10	0.15		
Magnesium	8	9.7	0.15		
Ammonium	37 (NH ₄ ⁺)	63 (NH ₃)	0.95 (NH ₃)		
<i>Anions</i>					
Chloride	100	355	5.33	562	99
Phosphate	25	74.5 (inorg. P)	1.12 (inorg. P)	6.1 (inorg. P)	82
Sulphate	40	64 (inorg. S)	0.96 (inorg. S)		
Organic acids	25				

The above average values, due to GAMBLE²¹, refer to an acid urine (pH 5.4) on an average diet, and are calculated on a 24-hour urine volume of 1500 ml. The values for the glomerular filtration were obtained by multiplying the filtration rate (137 l/24 hours, see the following page) by the average electrolyte levels in the serum ultrafiltrate. The electrolyte concentrations in the glomerular filtrate were calculated by means of the concentration ratios serum water/serum ultrafiltrate. According to PETERS³⁹ these ratios are: Na 0.91, K 0.82, Cl 1.03, PO₄-ion 1.2.

(b) Specific gravity

The specific gravity of urine is a measure of the total weight of dissolved substances, while the osmolality depends on the number of osmotically active particles present in the solution. The specific gravity and the milliosmolality (*the latter measured in practice by means of the quotient freezing-point depression/1.858 × 1000*) do not therefore necessarily always correspond. A sodium chloride solution has a lower specific gravity than an osmotically equivalent urea solution, i.e. one containing roughly the same number of particles. The aim of the concentration test is to assess the maximum osmotic capacity of the kidneys. A suitable measure of this function is the highest osmotic concentration which it is possible to attain. In clinical practice it is only for the sake of simplicity in the concentration test that the measurement of specific gravity is preferred to that of freezing-point depression

(SCHADE⁴⁴). The maximum concentration capacity of the human kidney^{40a} amounts to ca. 1400 mosm/l, corresponding to a freezing-point depression of 2.6°C. In evaluating the results of the concentration test in albuminuria, 1 unit of specific gravity must be subtracted per 3.9 g/l protein and per 2.7 g/l glucose⁵⁴.

Osmotic concentration values in urine and corresponding average specific gravities, on a mixed diet¹²

mosm/l	Spec. gravity	mosm/l	Spec. gravity
200	1.006	800	1.024
400	1.012	1000	1.030
600	1.018	1200	1.036

(c) Specific gravity and diuresis in isosthenuria

The following table shows for any given concentration capacity the minimum quantities of urine which are necessary for the elimination of the urinary constituents. The values are based on the graphical representation of DARROW¹² and a normal value of 1200 milliosmoles for the quantity of urinary constituents eliminated on a normal diet (GAMBLE²¹). The quantity of these substances is greatest on a protein-rich diet, smallest on a carbohydrate-rich diet. In fasting, ca. 800 milliosmoles of urinary constituents are eliminated⁵⁷; on a high-calorie, high-carbohydrate, low-protein diet, on which the breakdown of the bodily proteins is reduced, the quantity of these substances eliminated is lower still.

Maximum concentration capacity		Minimum quantity of urine in ml required for elimination of the urinary constituents from an intake of 100 Calories (after DARROW ¹²)		Minimum quantity of urine in ml required for elimination of 1200 milliosmoles of urinary constituents
Specific gravity	Milliosmoles per litre	Pure carbohydrate diet	Mixed diet	
1.006	ca. 200	ca. 105	ca. 160	ca. 6000
1.012	400	60	100	3000
1.018	600	40	70	2000
1.024	800	25	50	1500
1.030	1000	20	40	1200
1.036	1200	18	35	1000

* The potassium elimination, like that of the other electrolytes, is regulated by the tubular reabsorption. Potassium can, however, be eliminated by tubular secretion⁴, so that a hyperpotassaemia can only arise in cases of severe oliguria.

V. Renal function values (continued)

(d) Quantitative glomerular and tubular functioning tests

Renal plasma flow

Glomerular filtration

(after SMITH⁵⁰, not including the 24-hour glomerular filtrate of CAMARA et al.⁸, all values for a body surface area of 1.73 m²):

Glomerular filtration, inulin clearance method, short-duration tests:

men	131 ± 21.5 ml/min
women	117 ± 15.6 ml/min

Glomerular filtration in 24 hours, creatinine clearance method, normal physical activity⁸:

137 (113–150) litres
or 95.5 ml/min

Plasma urea clearance with a diuresis of over 2 ml/min = maximum clearance (*C_m*):

70.7 ml/min

The *C_m* value of 75 ml/min of PETERS and VAN SLYKE⁴⁰ which is often quoted relates to the *whole-blood* urea clearance in the determination of blood urea, and not the usual *plasma* urea clearance. The ratio of urea-*C_m* to glomerular filtrate, the latter measured by the inulin clearance method, is ca. 0.6. The urea-*C_m* is therefore not a measure of glomerular filtration like inulin clearance, since urea is in part reabsorbed from the tubules. With adequate tubular flow (*C_m*), however, the tubular urea reabsorption does not vary greatly, so that the urea clearance may be used clinically in assessing the glomerular filtration capacity. The "standard clearance" (*C_s*) with a diuresis of less than 2 ml/min bears no constant relation to the glomerular filtration and has therefore no diagnostic value.

Maximum values for tubular function

(after SMITH⁵⁰, all values for a body surface area of 1.73 m²):

Maximum tubular p-aminohippurate excretory capacity

(PAH-Tm):

men	79.8 ± 16.7 ml/min
women	77.2 ± 10.8 ml/min

Maximum tubular glucose reabsorptive capacity

(glucose-Tm):

men	375 ± 79.7 ml/min
women	303 ± 55.3 ml/min

These tests are a measure of the total mass of functioning tubular tissue.

Renal plasma flow

(after SMITH⁵⁰, as above):

Plasma minute-volume in functional kidney tissue

(PAH clearance):

men	654 ± 163 ml/min
women	592 ± 153 ml/min

Tubular secretion of phenolsulphonphthalein

According to SMITH⁵⁰ the phenol-red clearance amounts to 394 ± 45 ml/min. ROWNTREE and GERAGHTY's functioning test (quoted in ⁵⁴) can be performed in various ways^{54, 52a} and is based on the measurement of the percentage of an injected quantity of 6 mg phenolsulphonphthalein which is excreted in the urine during a certain period of time. During the first 65–70 min after injection 40–60% of the dye is normally excreted, during the next hour 20–25%.

Bibliography

Reviews: physical chemistry ^{16, 24, 44}; water and electrolyte balance ^{21, 31, 34, 39, 39a, 57}.

- 1) AHLMAN, K. L., et al., *J. clin. Endocr.*, **13**, 773, 1953.
- 2) ALBRITTON, E. C., *Standard Values in Blood*, Philadelphia, 1952.
- 3) BENNHOLD, H., KYLIN, E., and RUSZNYAK, S., *Die Eiweisskörper des Blutplasmas*, Dresden and Leipzig, 1938.
- 4) BERENSON, G. S., and BURCH, G. E., *J. Lab. clin. Med.*, **42**, 58, 1953.
- 5) BERGER, E. Y., et al., *Amer. J. Physiol.*, **162**, 318, 1950.
- 6) BERLINER, R. W., KENNEDY, T. J., and ORLOFF, J., *Amer. J. Med.*, **11**, 274, 1951.
- 7) BROCH, O. J., *Scand. J. clin. Lab. Invest.*, **5**, 9, 1953.
- 8) CAMARA, A. A., et al., *J. Lab. clin. Med.*, **37**, 743, 1951.
- 9) CARDOZO, R. H., and EDELMANN, I. S., *J. clin. Invest.*, **31**, 280, 1952.
- 10) CONN, J. W., *Arch. intern. Med.*, **83**, 416, 1949.
- 11) COOK, R. E., and CROWLEY, L. G., *N. Engl. J. Med.*, **246**, 637, 1952.
- 12) DARROW, D. C., and PRATT, E. L., *J. Amer. med. Ass.*, **143**, 364, 432, 1950.
- 13) DOUGLAS, C. G., and PRIESTLEY, J. G., *Human Physiology*, Oxford, 1948.
- 14) EDELMAN, I. S., et al., *Surg. Gynec. Obstet.*, **95**, 1, 1952.
- 15) EDELMAN, I. S., et al., *Science*, **115**, 447, 1952.
- 16) EDLBACHER, S., and LEUTHARDT, F., *Lehrbuch der physiologischen Chemie*, Berlin, 1952.
- 17) ESSELIER, A. F., JEANNERET, P., and ROSENEMUND, H., *Schweiz. med. Wschr.*, **83**, 727, 755, 1953.
- 18) FOLK, B. P., ZIERLER, K. L., and LILIENTHAL, J. L., *Amer. J. Physiol.*, **153**, 381, 1948.
- 19) FRAWLEY, F., and THORN, G. W., *Proc. Second Clinical ACTH Conference*, **1**, 115, Philadelphia and Toronto, 1951.
- 20) FRIIS-HANS, B. J., et al., *Pediatrics*, **7**, 321, 1951.
- 21) GAMBLE, J. L., *Chemical Anatomy, Physiology and Pathology of Extracellular Fluid*, Cambridge, Mass., 1953.
- 22) GIBSON, J. G., and EVANS, W. A., *J. clin. Invest.*, **16**, 317, 1937.
- 23) *Handbook of Chemistry and Physics*, Cleveland, 1954–55.
- 24) HOEBER, R., *Physikalische Chemie der Zellen und Gewebe*, Berne, 1947.
- 25) HURST, W. W., SCHEMM, F. R., and VOGEL, W. C., *J. Lab. clin. Med.*, **39**, 36, 1951.
- 26) *International Critical Tables*, New York, 1928.
- 27) JEANNERET, P., ROSENEMUND, H., and ESSELIER, A. F., *Helv. med. Acta*, **21**, 191, 1954.
- 28) LANDOLT-BOERNSTEIN, *Physikalisch-chemische Tabellen*, Berlin, 1923 et seq.
- 29) LEVITT, M. F., and GAUDINO, M., *Amer. J. Med.*, **9**, 208, 1950.
- 30) LOCKWOOD, J. S., and RANDALL, H. T., *Bull. N. Y. Acad. Med.*, **25**, 228, 1949.
- 31) MACH, R. S., *Les troubles du métabolisme du sel et de l'eau*, Lausanne and Paris, 1947.
- 32) MACH, R. S., *Schweiz. med. Wschr.*, **84**, 113, 1954.
- 33) MADDOCK, W. G., *Ohio St. med. J.*, **45**, 462, 1949.
- 34) MARIOTT, H. L., *Water and Salt Depletion*, Springfield, 1950.
- 35) MARTIN, L., *Gastroenterology*, **15**, 326, 1950.
- 36) MCCANCE, R. A., *Lancet*, **1**, 643, 704, 765, 833, 1936.
- 37) NEWBURGH, L. H., and JOHNSTON, M. W., *Physiol. Rev.*, **22**, 1, 1942.
- 38) PETERS, J. P., and VAN SLYKE, D. D., *Quantitative Clinical Chemistry*, Vol. II, *Methods*, London, 1932.
- 39) PETERS, J. P., *Body Water. The Exchange of Fluids in Man*, Springfield, 1935.
- 39a) PETERS, J. P., *Water Balance in Health and Disease*, in GARFIELD, G. P. (Edit.), *Diseases of Metabolism*, Philadelphia, 1953.
- 40) PETERS, J. P., and VAN SLYKE, D. D., *Quantitative Clinical Chemistry*, Vol. I, *Interpretations*, London, 1932.
- 40a) PITTS, R. F., and SARTORIUS, O. W., *Physiol. Rev.*, **2**, 161, 1950.
- 41) POLLARD, M. H., and BOLT, R. J., *Gastroenterology*, **22**, 564, 1952.
- 42) RANDALL, H. T., *Surg. Clin. N. Amer.*, **32**, 445, 1952.
- 43) SAEMUNDSSON, J., *Acta med. scand.*, Suppl. **208**, 1948.
- 44) SCHADE, H., *Die physikalische Chemie in der inneren Medizin*, Dresden and Leipzig, 1923.
- 45) SCHWARTZ, W. B., and RELMAN, A. S., *J. clin. Invest.*, **32**, 258, 1953.
- 46) SCRIBANTE, P., MAURICE, P., and FAVARGER, P., *Helv. physiol. pharmacol. Acta*, **10**, 224, 1953.
- 47) SCRIBNER, H., POWER, M. H., and RYNEARSON, E. H., *J. Amer. med. Ass.*, **144**, 1167, 1950.
- 48) SHOHL, A. T., *Mineral Metabolism*, New York, 1939.
- 49) VAN SLYKE, D. D., et al., *J. biol. Chem.*, **79**, 768, 1928.
- 50) SMITH, H. W., *The Kidney, Structure and Function in Health and Disease*, New York, 1951.
- 51) SOBERMAN, R., et al., *J. biol. Chem.*, **179**, 31, 1949.
- 52) SPUEHLER, O., *Quantitative Nierenfunktionsprüfungen*, in *Schweiz. Med. Jahrbuch*, Basle, 1951.
- 53) SUNDERMAN, F. W., *J. biol. Chem.*, **113**, 11, 1936.
- 54) SUNDERMAN, F. W., and BOERNER, F., *Normal Values in Clinical Medicine*, Philadelphia and London, 1950.
- 55) THORN, G. W., et al., *Amer. J. Med.*, **10**, 595, 1951.
- 56) WARMING-LARSEN, A., HAMBURGER, C., and SPRECHLER, M., *Acta endocr. (Kbh.)*, **11**, 400, 1952.
- 57) WEISBERG, H. F., *Water, Electrolyte and Acid-Base Balance*, Baltimore, 1953.
- 58) WHITE, A. G., GORDON, H., and LEITER, L., *J. clin. Invest.*, **29**, 1445, 1950.
- 59) WIGGERS, C. J., *Physiology in Health and Disease*, Philadelphia, 1949.
- 60) These *Tables*, page 287.
- 61) WUNDERLY, C., and WUHRMANN, F., *Schweiz. med. Wschr.*, **77**, 205, 1947.
- 62) These *Tables*, page 302.

(Normal values in seconds)

Distance	Time in seconds	Method of estimation	Remarks	Bibliography
Arm* → Foot	20–55 mean 43	²⁴ NaCl	In health (11 cases). In arteriosclerosis 20–105, mean 45 (24 cases); in arterio-sclerosis with diabetes 25–90, mean 42 (13 cases); in arteriosclerosis with diabetes and infection 20–40, mean 27 (5 cases); in thromboangiitis obliterans 20–70, mean 33 (12 cases); in chronic ulcerus cruris 30–45, mean 38 (3 cases); in hypertonia 20–80, mean 41 (13 cases).	SMITH and QUIMBY, <i>Surg. Gynec. Obstet.</i> , 79 , 142, 1944; <i>Radiology</i> , 45 , 335, 1945.
Arm* → Opposite hand				
Adults	17	²⁴ NaCl	Resting	HUBBARD et al., <i>J. clin. Invest.</i> , 21 , 613, 1942.
.....	13	²⁴ NaCl	After physical effort	
.....	23	²⁴ NaCl	With increased intrathoracic pressure (deep inspiration, glottis closed).	
Children:	11 (5–17) ...	²⁴ NaCl	Resting (22 cases)	SOHRNE, G., <i>Acta radiol.</i> , 26 , 279, 1945; HAMILTON and STONE, <i>Radiology</i> , 28 , 178, 1937 (quoted by HEVESY, G., <i>Radioactive Indicators</i> , New York, 1948).
Children:	7 (3–12) ...	²⁴ NaCl	Resting (14 cases)	
(2–12 years)				
Children:	7 (3–12) ...	²⁴ NaCl	Resting (14 cases)	
(6 weeks–22 months)				
Origin of femoral artery → End of tibial artery	22	²⁴ NaCl	Determination of this time is particularly valuable in deciding between a conservative therapy and operation, and above all in deciding the point of amputation (endarteritis obliterans). In rheumatoid arthritis the circulation in the extremities is slightly slower.	QUIMBY and SMITH, <i>Science</i> , 100 , 175, 1944; SMITH and QUIMBY, <i>ibid.</i> TOBIAS and BERTRAND, quoted by HEVESY, G., <i>Radioactive Indicators</i> , New York, 1948.
Arm* → Eye	7–15.6	Fluorescein	50 cases	FISHBACK et al., <i>Amer. J. med. Sci.</i> , 203 , 535, 1942.
Arm* → Lips	15–20	Fluorescein	212 cases	LANGE and BOYD, <i>Amer. J. med. Sci.</i> , 206 , 438, 1943.
Arm* → Nail-groove capillaries of other arm	16–20	Trypaflavin	36 cases	DONAT and PIRTKIEN, <i>Klin. Wschr.</i> , 31 , 670, 1953.
	mean 17.4			
Arm* → Tongue	9–16	Saccharin	100 cases	FISCHBERG et al., <i>Proc. Soc. exp. Biol.</i> , 30 , 651, 1933.
	10–16	Decholin	60 cases	TARR et al., <i>Amer. Heart J.</i> , 8 , 766, 1933.
	9–16	Calcium gluconate .	21 cases	BAER and SLIPAKOFF, <i>Amer. Heart J.</i> 16 , 29, 1938.
Arm* → Throat	7–17.8	Magnesium sulphate	92 cases	BERNSTEIN and SIMKINS, <i>Amer. Heart J.</i> , 17 , 218, 1939.
Arm* → Lungs	3– 8	Ether	164 cases	HITZIG, W. M., <i>Amer. Heart J.</i> , 10 , 1080, 1935.
Arm* → Respiration centre	6.4–12.1	α -Lobeline	545 cases	See footnote ¹ .
	mean 9.26, standard deviation σ 1.43			
	15.4–27.0	Papaverine	50 cases	ELEK and SOLARZ, <i>Amer. Heart J.</i> , 24 , 821, 1942.
Lungs → Respiration centre	5–10	CO ₂	30 cases	GUBNER et al., <i>J. clin. Invest.</i> , 18 , 395, 1939.
Lungs → Face	14–25	Amyl nitrate	100 cases	GROSS, D., <i>Amer. Heart J.</i> , 30 , 19, 1945.

* Arm = antecubital vein.

¹) Calculated from data from the following sources: BERLINER, K., *Arch. intern. Med.*, **65**, 896, 1940. BILIMOVIC, A., *Z. Kreislforsch.*, **34**, 51, 1942. EWZLINA, M. M., *Urač. Delo*, **20**, 113, 1938. FIGUEIREDO MAGALHAES and DE MESQUITA, *Brasil-med.*, **56**, 201, 1942. KADENAS, N., *Wien. med. Wschr.*, **33**, 661, 1940. LILIENTHAL and BERLINER, *Arch. intern. Med.*, **69**, 739, 1942. LOLOW, W., *Isledwaniia warchu zirkulazionoto wreme u zdrowii i sardetschno bolniia tchowiek*, Vol. 1, Sofia, 1946. MASBERNARD and CAMELIN, *Klin. Wschr.*, **31**, 455, 1953. MOSCO, D., *Endocrinologia*, **15**, 3, 1940. MOSCO, D., *Boll. Soc. med.-chir. Modena*, **42**, 3, 1941–42. MOSCO and CAMPANI, *ibid.*, **42**, 355, 1941–42. PICCIONE and BOYD, *J. Lab. clin. Med.*, **26**, 766, 1940. PLASVIC, C., *Arch. Mal. Cœur*, **32**, 163, 1939. TIPOV and SCHOR, *Ter. Arkh.* (USSR), **13**, 57, 1935. VOLGIN et al., *Med. Pregl.*, **5**, 90, 1939.

Arterial blood pressure in mm Hg (normal range and hypertonic limits)

Systolic					Diastolic				
Age	Normal range		Lower hyper-tonic limit		Age	Normal range		Lower hyper-tonic limit	
	Men	Women	Men	Women		Men	Women	Men	Women
16	105–135	100–130	145	140	16	60–86	60–85	90	90
17	105–135	100–130	145	140	17	60–86	60–85	90	90
18	105–135	100–130	145	140	18	60–86	60–85	90	90
19	105–140	100–130	150	140	19	60–88	60–85	95	90
20–24	105–140	100–130	150	140	20–24	62–88	60–85	95	90
25–29	108–140	102–130	150	140	25–29	65–90	60–86	96	92
30–34	110–145	102–135	155	145	30–34	68–92	60–88	98	95
35–39	110–145	105–140	160	150	35–39	68–92	65–90	100	98
40–44	110–150	105–150	165	165	40–44	70–94	65–92	100	100
45–49	110–155	105–155	170	175	45–49	70–96	65–96	104	105
50–54	115–160	110–165	175	180	50–54	70–98	70–100	106	108
55–59	115–165	110–170	180	185	55–59	70–98	70–100	108	108
60–64	115–170	115–175	190	190	60–64	70–100	70–100	110	110

in healthy persons as well as those with circulatory disturbances (RUEGER, H. J., *Ann. intern. Med.*, **35**, 1023, 1951).

Clinical forms of hypertension

1. Essential hypertension (genuine, “red” hypertension). AfterVOLHARD, F., *Blutdruck und Niere*, in BECKER, E., *Nierenkrankheiten*, Jena, 1944.

Characteristics: marked increase in systolic pressure with relatively small increase in diastolic pressure (large pressure difference); no perceptible renal participation, fairly amenable to treatment by a salt-free diet, rest in bed and sedatives; reddish or reddish-blue face (according to BERGLUND, HAMMARSTRÖM and WERKÖ, *Verh. dtsch. Ges. Kreisl.-Forsch.*, 1949, the latter is due to dilatation of the venous capillaries while the arterial capillaries are contracted). – Increase of blood pressure in essential hypertension is due to diminished elasticity of the large arteries and to a more or less marked increase in peripheral resistance (due to constriction of the arterioles). The origins of these changes are unknown but are presumably linked with a regulatory disturbance involving principally the hypothalamus, the sympathicus and the endocrine system. The presence of pressor substances such as those associated with nephrogenic hypertension, for example, has not yet been demonstrated with certainty. – As a result of the injury to the kidneys, essential hypertension of long duration is eventually accompanied by nephrogenic hypertension.

2. Renal hypertension

(a) Hypertension in chronic inflammation of the kidneys and nephrosclerosis (white hypertension).

Characteristics: continuous hypertension with a large increase in the diastolic pressure, facial pallor, angiospastic retinitis, adrenal insufficiency. – The increase in blood pressure is due principally to a general narrowing of the arterioles: resistance pressure. – In this form of hypertension the presence of pressor substances has been demonstrated (renin, hypertensinogen, nephrine); it is doubtful, however, whether these are the actual vasopressor substances since their hypertensive effect falls to zero after repeated injections.

(b) Hypertension in acute glomerular nephritis.

Characteristics: general constriction of the arterioles and capillaries: increase in the peripheral resistance. Increased blood pressure is often the first symptom in acute glomerular nephritis and precedes the injury to the kidneys (allergic reaction?). In the transition from acute to chronic glomerular nephritis an ischaemia and renal hypertension develops along with the hyalinization of the glomeruli.

An increase of blood pressure precedes kidney injury in eclampsia also.

In all cases of hypertension each kidney should be separately examined since the cause is frequently unilateral kidney injury. In such cases operative treatment (lowering of the blood pressure after removal of the affected kidney) is often successful. – See above for other forms of hypertension.

Pressure (in mm Hg)

Venous blood pressure 2.9–8.1

Methods of measurement: With membrane manometers (WIGGERS, C. J., *The Pressure Pulses in the Cardiovascular System, Monographs on Physiology*, London, 1928; MÜLLER et al., *Helv. physiol. pharmacol. Acta*, **6**, 783, 1948; TYBJAERG HANSEN and WARBURG, *Acta physiol. scand.*, **19**, 306, 1950; TYBJAERG HANSEN, A., *ibid.*, **19**, 333, 1950), photoelectric manometers (REIN et al., *Arch. Physiol.*, **243**, 329, 1940), piezoelectric manometers (LANGEVIN and GOMEZ, C. R. *Soc. Biol.*, **113**, 1126, 1933; MACLEOD and COHN, *Amer. Heart J.*, **21**, 345, 1941), induction manometers (WETTER, E., *Z. Biol.*, **101**, 332, 1944), magnetolectric manometers (HAMPEL, A., *Arch. Physiol.*, **244**, 171, 1941), resistance manometers (BRAUNSTEIN et al., *Science*, **105**, 267, 1947; LAMBERT and WOOD, *Proc. Soc. exp. Biol.*, **64**, 186, 1947), capacity manometers (TYBJAERG HANSEN and WARBURG, *Amer. Heart J.*, **33**, 709, 1947; TYBJAERG HANSEN, A., *Pressure Measurement in the Human Organism*, Copenhagen, 1949) and membrane manometers with electronic transmission (CLEMENDSON and PETTERSSON, *J. Lab. clin. Med.*, **38**, 631, 1951).

Blood pressure in the capillaries of the hand (hand at the level of the heart)

with bleeding

arterial capillaries ~ 32 } LANDIS, E. M., *Amer. J. Physiol.*, **75**, 548, 1925–26; *Heart*, **15**, 209, 1930.

without bleeding (2500 measurements)

capillaries 27.2 ± 4.4 } KÜCHMEISTER, H., *Ergebn. inn. Med. Kinderheilk.*, **4**, 462, 1953.

arterioles 47.1 ± 2.2

Right atrial mean pressure – 2 to + 5

Right ventricular pressure

peak systole 17 to 31.5

end diastole – 0.5 to + 7

Pulmonary arterial pressure

peak systole 11 to 29

end diastole 4 to 13

mean 8 to 19

Pulmonary “capillary” pressure

mean 5 to 13

Method

Indirect (RIVA-ROCCI apparatus). Values measured indirectly agree with those measured directly (STEELE, J. M., *J. Mt Sinai Hosp.*, **8**, 1042, 1942). Direct measurement with the manometric apparatus of HAMILTON, BREWER and BROTMANN, *Amer. J. Physiol.*, **107**, 427, 1934. In the initial examination the precaution should be taken of measuring the blood pressure on both arms since significant differences between the two arms are often observed (systolic and diastolic)

Remarks

Values from MASTER, A. M., et al., *Bull. N. Y. Acad. Sci.*, **27**, 452, 1951, and MASTER et al., *Normal Blood Pressure and Hypertension*, Philadelphia, 1952. Hypertension in adults: see the adjacent table. With a systolic pressure under 170 mm there is no danger of haemorrhage. A diastolic pressure over 130 mm is dangerous.

Blood pressure is temporarily increased after physical exercise (5–10 min), in emotional excitement (systolic pressure only, duration variable), in acute nephritis (several weeks), in eclampsia, in the menopause (months, years or permanently). Continuous high blood pressure is shown in essential hypertension; in certain kidney diseases (nephrosclerosis, in the later stages of subacute glomerular nephritis, as a result of pyelonephritis or in pressure damage to the kidneys, e.g. owing to urinary stasis or enlarged prostate); in endocrine disturbances (pituitary; adrenals: excessive adrenocortical hormone production usually leads to continuous high-level adrenaline liberation rather than to paroxysmal increases of blood pressure); in arteriosclerosis; with increased blood viscosity (e.g. in polycythaemia); in increased intracranial pressure; in obesity; in certain myocardial lesions (right atrium): pressure increase due to back pressure.

Blood pressure is temporarily lowered in shock and collapse, after severe haemorrhages, in diarrhoea; continuous low pressure may be constitutional (asthenia, debility) or due to endocrine disturbances, myocardial degeneration, chronic anaemia.

The venous blood pressure is dependent on the distance from the heart (highest pressure at the periphery). The blood pressure in the veins is the algebraic sum of the positive residual arterial pressure and the negative pressure exerted on the column of blood by the thoracic cavity. It varies in accordance with the position of the vein with respect to the right atrium as a result of the different effect of gravity.

The venous blood pressure in the capillaries is lower than the osmotic pressure of the plasma.

Summarized by FOWLER et al., *Amer. Heart J.*, **46**, 264, 1953, from measurements on a total of 72 subjects.

Pressures in the right heart measured by catheterization in the manner of COURNAND and RANGES, *Proc. Soc. exp. Biol.*, **46**, 462, 1941.

(20/20° C)

	Normal value	Method	Remarks
Whole blood			
Men	1.055–1.062	After LOWRY, see BESSEY, O. A., <i>Microchemical Methods</i> , in GYÖRGY, P., <i>Vitamin Methods</i> , New York, 1950. VAN SLYKE'S copper sulphate method.	The specific gravity of the blood rises and falls with the total number of cell elements (mean specific gravity of erythrocytes ca. 1.983, see page 335).
Women	1.050–1.056		
Plasma	1.025–1.029	„	The specific gravity of the plasma and serum rises and falls with the protein content. <i>Specific gravity lowered:</i> (blood) in anaemia; (plasma) in marasmus, hydropic renal disease. <i>Specific gravity increased:</i> (blood) polycythaemia; (plasma) cholera, dysentery, severe burns, plasmocytoma (myeloma).
Serum	1.024–1.028	„	

Specific gravity / Serum water / Solid components¹

The following table allows the conversion of

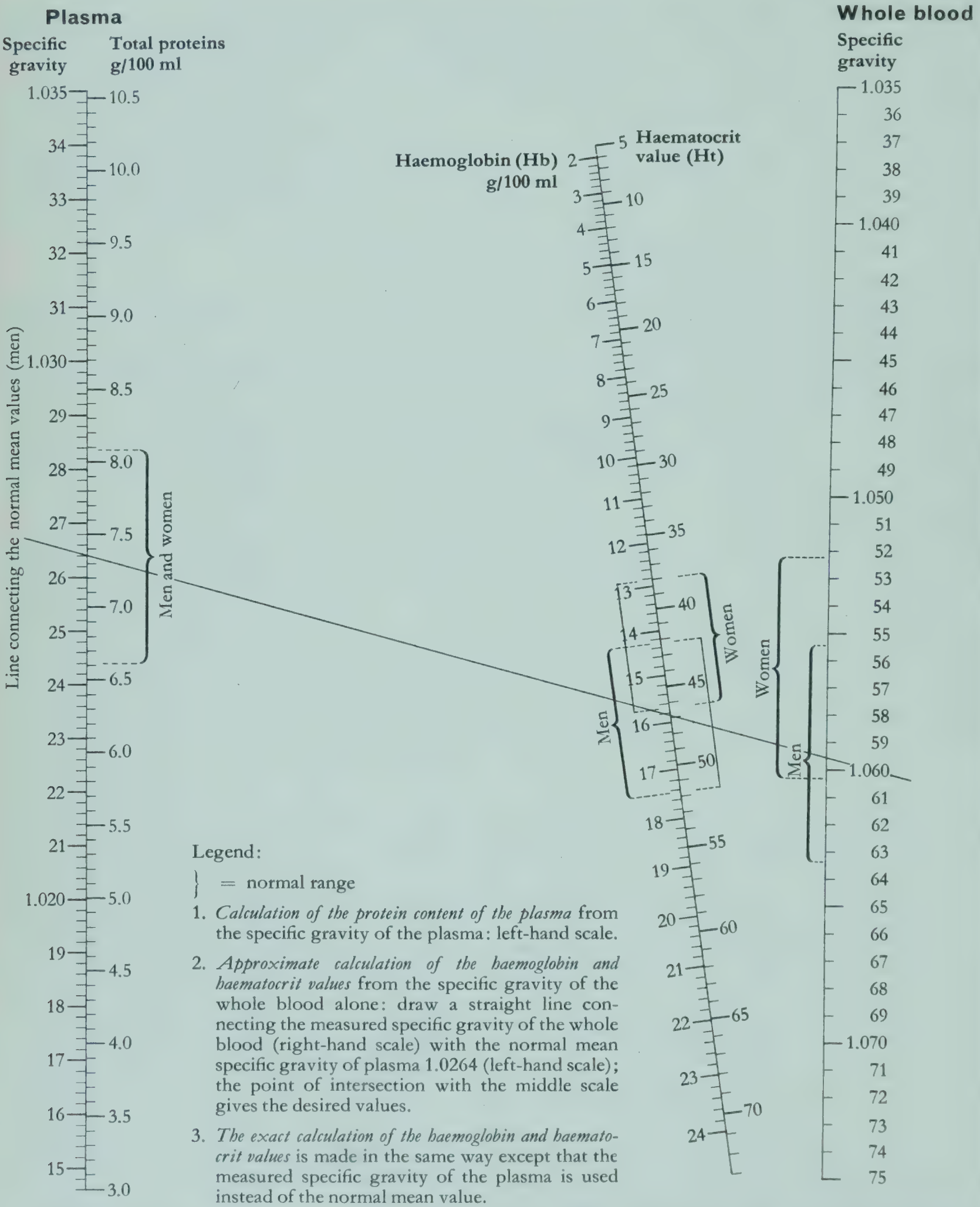
(a) the concentration of a substance in 1 litre of serum into its concentration in 1 kg of serum water, i.e. the molality (multiplication by the factor in column 6), and

(b) the concentration of a substance in 1 kg of serum water into its concentration in 1 litre of serum (multiplication by the factor in column 4 and division by 1000).

Specific gravity	Water per kilogram serum (grams)	Solid components per kilogram serum (grams)	Water per litre serum (grams)	Solid components per litre serum (grams)	Multiplication factor
1.015	952	48	966	34	1.035
1.016	948	52	964	36	1.038
1.017	945	55	961	39	1.040
1.018	942	58	959	41	1.043
1.019	939	61	957	43	1.045
1.020	936	64	954	46	1.048
1.021	932	68	952	48	1.051
1.022	929	71	949	51	1.053
1.023	926	74	947	53	1.056
1.024	923	77	945	55	1.059
1.025	919	81	942	58	1.061
1.026	916	84	940	60	1.064
1.027	913	87	938	62	1.067
1.028	910	90	935	65	1.069
1.029	906	94	933	67	1.072
1.030	903	97	930	70	1.075
1.031	900	100	928	72	1.078
1.032	897	103	925	75	1.081
1.033	894	106	923	78	1.083
1.034	890	110	921	79	1.086

¹) After SUNDERMAN, F. W., *J. biol. Chem.*, 113, 1, 1936.

Nomogram for the calculation of the haemoglobin and haematocrit values and of the protein content of the plasma from the specific gravity of the whole blood and the plasma (or from that of the whole blood alone)¹



Correction for oxalated blood : subtract from the measured specific gravities of the whole blood and plasma 0.0004 for each milligram of the 3:2 ammonium oxalate/potassium oxalate mixture which has been added per millilitre of the blood (for specific gravity related to water at the same temperature).

¹) After PHILIPS et al., Bull. U.S. Army med. Dep., No. 71, 1943.

Normal values

(For definition of the normal range, see footnote page 317)

Total volume (in millilitres per kilogram body weight)
(men and women as one group)

Method	Whole blood		
	Mean	Normal range (mean \pm 2 σ)	Standard deviation σ
(1)	65.6	51.0–81.2	7.3
(2)	71.4	55.6–87.2	7.9
(3)	69.8	51.2–86.4	8.3
	Erythrocytes		
(1)	25.8	20.4–31.2	2.7
(2)	30.3	19.1–41.5	5.6
(3)	27.7	21.5–32.9	3.6
	Plasma		
(1)	39.8	27.6–52.0	6.1
(2)	41.1	29.9–52.3	5.6
(3)	42.1	30.5–53.7	5.8
	Ratio of total haematocrit to venous haematocrit		
(4)	0.910	0.905–0.915	0.026

Remarks

Physiological variations: the total blood volume at birth is ca. 300 ml and doubles itself during the first year of life¹. Subsequently it increases gradually in proportion to bodily development up to puberty. Values are equal for boys and girls up to puberty, subsequently those for boys increase more rapidly than those for girls. The total blood and plasma volumes are closely dependent on bodily dimensions and bear little relation to age².

The total blood volume remains relatively constant; after oral or intravenous intake of liquid the normal level is regained rapidly³. Rest in bed brings about a reduction in the total blood volume, mainly as a result of diminished plasma volume⁴. In both men and women athletics leads to an increased total blood volume and an increase in haemoglobin⁵. Plasma and blood volumes both increase during pregnancy^{6,7} (see page 272).

Pathological variations: greatly increased total blood and erythrocyte volumes are characteristic signs of erythraemia^{8,9}. Total erythrocyte volumes of 48.8–93.9 ml/kg body weight have been observed in this disease¹⁰, with a simultaneous reduction of plasma volume to 29ml/kg on the average. Plasma vol-

Methods and bibliography

(1) Determined by means of ³²P-labelled erythrocytes, values from WASSERMAN et al., *J. Lab. clin. Med.*, **37**, 342, 1951.

(2) Determined by simultaneous labelling of the erythrocytes with radioactive sodium chromate and of the plasma with radioactive chromic chloride. After GRAY and FRANK, *J. clin. Invest.*, **32**, 1000, 1953.

(3) Determined by the dyestuff dilution method, values from WASSERMAN, *loc. cit.* Literature on dyestuff methods: Geigy Blue 536: SOMOGYI, J. C., *Schweiz. med. Wschr.*, **71**, 225, 1941; SCHNEIDER, J. A., *Z. ges. inn. Med.*, **5**, 124, 1950; Evans blue (T 1824): GREGERSEN et al., *Amer. J. Physiol.*, **113**, 54, 1935; CROOKE and MORRIS, *J. Physiol.*, **101**, 217, 1942; WASSERMAN, *loc. cit.* – CO-method (marking of the erythrocytes with CO) and also a comparison with dyestuff methods: HOPPER et al., *J. clin. Invest.*, **23**, 628, 636, 1944. – ³²P-Method: WASSERMAN, *loc. cit.*; MUKHERJEE and ROWLANDS, *Lancet*, **2**, 98, 1951.

(4) After CHAPLIN et al., *J. clin. Invest.*, **32**, 1309, 1953, in agreement with others.

The ³²P-methods are more accurate than the dyestuff methods for determination of total blood volume since centrifuging is avoided. The latter methods give rather larger values than those using ³²P.

ume is decreased in nephrosis and increased under ACTH or adrenocortical hormone therapy (cf. Corticotropin, page 186), as also in cardiac disease with severe decompensation¹¹. A marked reduction in total blood volume accompanies shock, acute haemorrhages and dehydration; mercury diuretics bring about a decrease, theophylline derivatives an increase, of plasma volume¹². Earlier data (prior to ca. 1935) on blood volume variations in pathological conditions should be treated with reserve since former methods of measurement lacked the accuracy of the present-day isotope and dyestuff methods¹³.

The ratio of the total erythrocyte volume to the total blood volume (total haematocrit value) is less than the venous haematocrit value. If the total blood volume is calculated from the total plasma volume and the venous haematocrit value, the latter must accordingly be multiplied by the correction factor 0.91. It is safer, however, to determine simultaneously the total plasma and erythrocyte volumes by method (2) above.

For a review of the total plasma volume, see SÖSTRAND, T., *Physiol. Rev.*, **33**, 202, 1953; or BERLIN et al., *New Engl. J. Med.*, **247**, 675, 1952.

Normal values

Osmotic pressure

(at 0°C) (serum) 6.47–6.72; mean 6.62 atm equal to 4922–5106 mm Hg; mean 5030 mm Hg

Colloid-osmotic pressure (at 0°C) (serum)

20.59–35.30 mm Hg; mean 24.71 mm Hg equal to 280–480 mm H₂O; mean 330 mm H₂O

Freezing-point

depression (serum) ... 0.535–0.555°C; mean 0.547°C

Methods and bibliography

Calculated from the freezing-point depression (cf. pages 114–116) or measured directly.

Values from KEYS and HILL, *J. exp. Biol.*, **11**, 28, 1934, in agreement with more recent methods using osmotic balances: JULANDER and SVEDBERG, *Nature (Lond.)*, **153**, 523, 1944; with osmometer: BOURDILLON, J., *J. biol. Chem.*, **127**, 617, 1939; CLEMENT, P., *Bull. Soc. chim. Fr.*, 781, 1949; HOLM-JENSEN, I., *Scand. J. clin. Lab. Invest.*, **1**, 87, 1949.

By cryoscope. Values from SUNDERMAN and BOERNER, *Normal Values in Clinical Medicine*, Philadelphia, 1950. After GRAM, H. C., *Amer. J. med. Sci.*, **168**, 511, 1924: range 0.555 to 0.570, mean 0.562°C.

Remarks

Mainly due to the crystalloid constituents; ca. 0.5% of the total osmotic pressure is due to the colloidal constituents.

The colloid-osmotic pressure (COP) amounts to ca. 1/200 of the total osmotic pressure and can be calculated approximately from the serum albumin and globulin values. COP in mm H₂O (at 0°C) = f(45.2A + 18.8G), where A = albumin value and G = globulin value in grams %, and f is a factor dependent on the total protein serum value¹⁴ (total protein = 2%, f = 0.92; = 4%, f = 1.03; = 6%, f = 1.17; = 8%, f = 1.45). Most of the colloid-osmotic pressure is due to albumin; fibrinogen exerts no measurable coll.-osm. pressure. In the organism the coll.-osm. pressure is maintained constant; WUHRMANN and WUNDERLY^{15,16}, in common with other workers^{18,19} ascribe this to an appropriate regulation of the serum albumin level.

→ On osmotic pressure and freezing-point depression see pages 114–116.

¹) BRINES et al., *J. Pediat.*, **18**, 447, 1941. ²) RUSSEL, S. J. M., *Arch. Dis. Childh.*, **24**, 88, 1949. ³) KALTREIDER and MENEELY, *J. clin. Invest.*, **19**, 627, 1940. ⁴) TAYLOR et al., *Amer. J. Physiol.*, **144**, 227, 1945. ⁵) KYELLBERG et al., *Acta physiol. scand.*, **19**, 146, 1949. ⁶) THOMSON et al., *Amer. J. Gynec.*, **36**, 48, 1938. ⁷) MOORE et al., *Amer. J. Gynec.*, **57**, 481, 1949. ⁸) GIBSON et al., *J. clin. Invest.*, **18**, 621, 1939. ⁹) HADEN, R., *Amer. J. med. Sci.*, **196**, 493, 1938. ¹⁰) BERLIN et al., *Amer. J. Med.*, **9**, 747, 1950. ¹¹) SPÜHLER et al., *Helv. med. Acta*, **15**, 95, 1948. ¹²) WINTROBE, M. M., *Clinical Hematology*, Philadelphia, 1952. ¹³) KEYS, A., *J. phys. Chem.*, **42**, 11, 1938. ¹⁴) WUHRMANN and WUNDERLY, *Schweiz. med. Wschr.*, **75**, 234, 1945. ¹⁵) BJØRNEBOE, M., *Acta path. microbiol. scand.*, **22**, 323, 1945. ¹⁶) BJØRNEBOE, M., *Acta med. scand.*, **123**, 393, 1946. ¹⁷) BING, J., *Nord. Med.*, **29**, 1455, 1945. ¹⁸) WUHRMANN and WUNDERLY, *Die Bluteiweisskörper des Menschen*, Basle, 1952.

Normal values

(For definition of the normal range, see footnote page 317)

Viscosity

(1) Relative viscosity (viscosity of water = 1) measured *in vitro*

Whole blood: 3.5–5.4; mean: women 4.5 men 5.0

Plasma: 1.9–2.3
Serum: 1.6–2.2

(2) Absolute viscosity *in vivo*, expressed in centipoises:

Whole blood: 2.46–2.94; mean 2.70
standard deviation 0.12

Methods: (1) by HESS viscosimeter with GRAM's temperature correction (HESS, W. R., *Viskosität des Blutes, Vjschr. naturf. Ges. Zürich*, 1906; GRAM, H. C., *Amer. J. med. Sci.*, 168, 511, 1924). (2) from PIROFSKY, B., *J. clin. Invest.*, 32, 992, 1953.

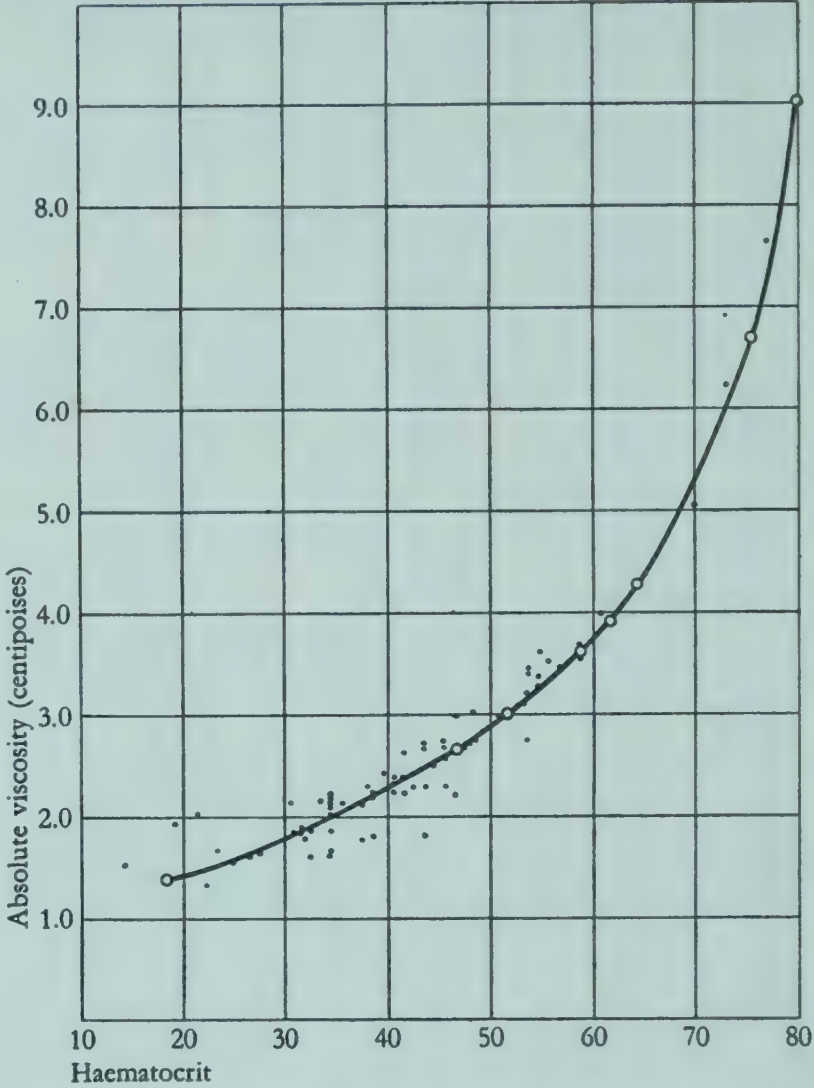
Remarks: The relative viscosity of whole blood measured *in vitro* by HESS's method (*loc. cit.*) is not always in agreement with the absolute viscosity *in vivo*, and cannot therefore be used in haemodynamic calculations. The absolute viscosity *in vivo* may be measured quite simply by PIROFSKY's method (*loc. cit.*).

The viscosity of whole blood is primarily dependent on the blood-corpuscle content, i.e. in health on the erythrocyte content. The viscosity of plasma is due to the protein content, primarily the fibrinogen and globulins.

The viscosity is also affected by the CO₂ content (venous blood is more viscous than arterial blood), by the form of the erythrocytes, the presence of abnormal plasma proteins, and other factors.

The viscosity is increased in polycythaemia vera, in leukaemia¹, in cryoglobulinaemia², by changes in the plasma protein values³, in sickle-cell anaemia⁴, in hypercholesterinaemia⁵, in hyperglycaemia⁶.

The blood of women has normally a somewhat lower viscosity than that of men, and that of children a lower viscosity than that of adults.



Relation between haematocrit value and absolute viscosity of normal blood (after PIROFSKY, *loc. cit.*).

Sedimentation rate (erythrocyte sedimentation rate,ESR) (mornings, fasting)

	WESTERGREN methods			LINZENMEIER's method ¹⁰
	Original ⁷	ALDER's "wide tube" modification ⁸	WINTROBE's modification ⁹	
Sedimentation tube				
Blood column	200 mm	100 mm	100 mm	50 mm
Diameter	2.5 mm	5 mm	2.5 mm	5 mm
Anticoagulant	Sodium citrate 3.8% soln.	Sodium citrate 3.8% soln.	2 parts potassium oxalate + 3 parts ammonium oxalate dry	Sodium citrate 5% soln.
Quantity (mg/100 ml mixture) ...	760	760	200	1000
Resulting dilution of blood	20%	20%	0	20%
Method of reading	Sedimentation in 1, 2 or 24 hours	Sedimentation in 1 or 2 hours	Sedimentation in 1 hour	Time for a sedimentation of 18 mm
Normal values 1 hour				} 200–600 minutes — see below
Adults: Men	up to 7 mm	up to 6 mm	up to 6.5 mm; mean 3.7 mm	
Women	up to 11 mm	up to 7 mm	up to 15 mm; mean 9.6 mm	
Adolescents 12–20 years ¹¹	—	—	up to 20 mm; mean 4.7 mm	
Newborn	up to 2 mm ¹¹	—	up to 2 mm ¹¹	
Normal values 2 hours			Values for infants by LINZENMEIER's method ¹²	
Adults: Men	up to 8 mm	up to 18 mm	Age	Mean (hours)
Women	up to 16 mm	up to 20 mm		Range (hours)
Normal values 24 hours			1 day	106
Adults: Men	up to 50 mm		2 days	57
Women	up to 70 mm		4 days	45
			6 days	20
			8 days	14
			9–14 days	10
			9–12 months	1¼
Normal values 24 hours (tube inclined at 45° after 2 hours)			Micromethods (WESTERGREN): CUTLER ¹³ , SMITH ¹¹ , etc.	
Men	up to 90 mm			
Women	up to 110 mm			

¹) STEPHENS, D., *Proc. Soc. exp. Biol.*, 35, 251, 1936. ²) PETERSEN, E., *J. Lab. clin. Med.*, 42, 641, 1953. ³) CHOPRA and CHOUDHURY, *Indian J. med. Res.*, 16, 939, 1929. ⁴) MCCORD et al., *Proc. Soc. exp. Biol.*, 69, 19, 1948. ⁵) BURTON-OPITZ, R., *J. exp. Med.*, 8, 240, 1906. ⁶) FISHBERG, E. H., *J. biol. Chem.*, 85, 465, 1930. ⁷) WESTERGREN, A., *Ergebn. inn. Med. Kinderheilk.*, 26, 577, 1924. ⁸) ALDER, A., Aarhus, unpublished. ⁹) WINTROBE and LANDSBERG, *Amer. J. med. Sci.*, 189, 102, 1935. ¹⁰) LINZENMEIER, G., *Arch. Gynäk.*, 113, 608, 1920. ¹¹) SMITH, C. H., *Amer. J. med. Sci.*, 192, 73, 1936. ¹²) HURWITZ et al., *J. Pediat.*, 12, 785, 1938. ¹³) CUTLER, J. W., *J. Lab. clin. Med.*, 26, 542, 1940.

Normal values

(For definition of the normal range, see footnote page 317)

Sedimentation rate (erythrocyte sedimentation rate, ESR – continued)
(mornings, fasting)

Remarks

The mechanism of the erythrocyte sedimentation reaction is only partly understood. In the first place the plasma proteins have a decisive effect, above all the fibrinogen, which has by far the greatest accelerating effect on the ESR^{1,2}. The effects of fibrinogen, euglobulin, pseudoglobulin and albumin are in the ratio 100:20:2:1.5³. There is a close correlation between globulin and ESR^{4,5}, particularly in liver diseases, in which there is a lowering of the serum fibrinogen. In the second place the ESR is influenced by the number, the haemoglobin content, the form and size of the erythrocytes⁶, as well as by the lipid content of the plasma. On the other hand there is no observable relationship between the ESR and the sugar, O₂ and CO₂, calcium and phosphorus content of the blood^{7,8}. The rouleau formation of the erythrocytes, which is the most important factor in the increase of ESR in disease and pregnancy¹⁰, is probably the result of a flocculation reaction between the plasma proteins and the lecithoprotein surface of the erythrocytes⁹. All the above remarks apply to measurements with exactly vertical sedimentation tubes. Even the slightest deviation from the vertical causes a marked increase in the observed ESR.

Physiological variations: for reasons unknown the sedimentation reaction is more constant in men than in women (menstruation has only a small, clinically insignificant effect on this difference¹⁰). In pregnancy the ESR begins to increase at the 10th–12th week and returns to normal only by the 3rd–4th week after parturition^{7,8}. The ESR increases with advancing age¹¹.

Pathological variations: often retarded in polycythaemia, cardiac obstruction, disease of the liver parenchyma, acute anaphylactic conditions, vagotonia. Usually increased in all inflammations, in acute or active chronic infections (tuberculosis), in diseases accompanied by necrosis and tissue degradation; after ultra-violet or X-irradiation or stimulation therapy.

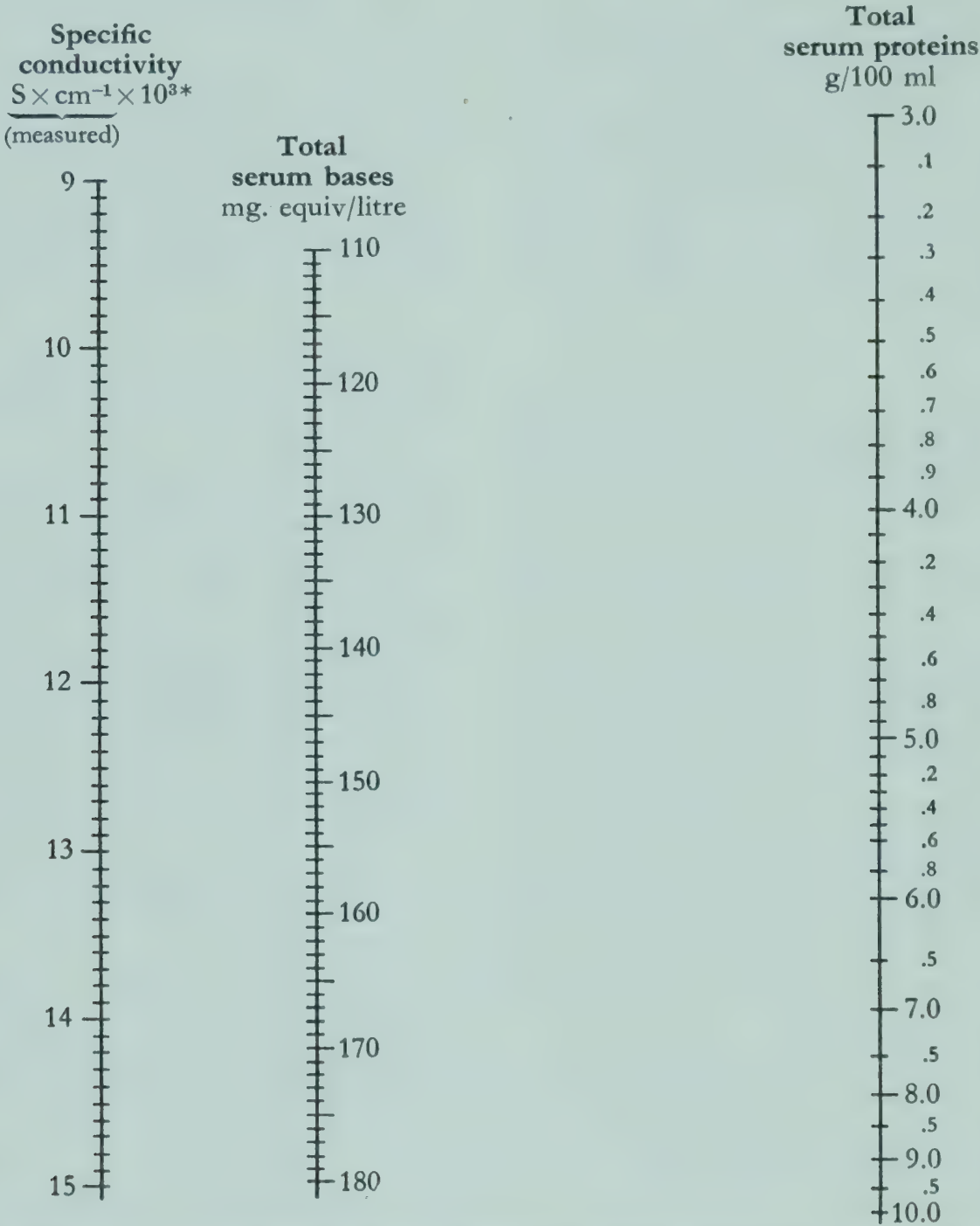
Guiding principles for practice¹² (WESTERGREN methods)

1. In principle no more information can be expected from the ESR than this simple, non-specific, routine method is capable of offering to the practitioner at the sick-bed. Even when the ESR is normal a thorough examination cannot be dispensed with. In contrast to the rapidly reacting blood picture the ESR usually reacts with a delay of 20–30 hours.
2. In the great majority of cases an increase in the ESR is due to a displacement in the blood proteins; only very rarely is it due to cellular changes (number, form, surface, etc. of erythrocytes).
3. The ESR shows hardly any variation during the course of the day so that any major changes are of significance; the usual 1- and 2-hour values generally suffice, the normal values varying somewhat according to the method. In view of the differences between individuals it is important to know exactly the patient's minimum values. Greatly increased 2-hour values with normal 1-hour values are rare but occur particularly in hepatic disease.
4. A distinct increase in the ESR is an indication under any circumstances of a pathological condition, although it cannot be assumed to point to any particular disease (persistence during convalescence or the postoperative period). When no cause of a distinct increase in ESR can be found the examination must be taken a stage further. In the case of large increases, such as 1-hour values of 50 mm or more, the 2-hour values are very little higher and the absolute value of the increase is of little significance.
5. An exceptionally large initial increase in ESR, where a maximum value of 70 mm or more is reached in 15–20 minutes, points strongly to a plasmocytoma (myeloma) or a macroglobulinaemia.
6. A normal ESR never excludes the possibility of disease, even those with severe evolution such as tuberculosis or carcinoma; in particular an increase in ESR is often delayed for a considerable time by haemodynamic decompensation.
7. Lack of an increase in ESR may be taken as confirmation of an otherwise negative clinical picture and the ESR value deserves to be more widely used in routine medical examinations.
8. A single measurement of ESR can be misleading in several ways: too little citrate accelerates, too much retards. High temperatures can likewise have an accelerating effect. In case of doubt it may be advisable to repeat the test at short intervals.
9. The full significance of an ESR measured at the climax of a disease is only apparent in comparison with later measurements; in an acute disease there is little point in making an ESR measurement if it can only be evaluated by waiting until the ESR has in any case returned to normal (cf. measurement of temperature in fever).
10. On the other hand the great value of the ESR may be lost by the creation of a "sedimentation" neurosis due to too frequent repetition.
11. The ESR is often less affected by the basic disease than by the secondary complications, such as pneumonia, pleurisy, thrombophlebitis, arthritic components, intercurrent infections, etc.
12. Since the ESR yields diagnostic indications it is equally valuable by the prognostic and therapeutic points of view; in practice it is one of the most useful aids in triage.
13. The secondary results of an ESR measurement, such as the appearance of the plasma in the sedimentation tube, presence of pathological cell aggregations (e.g. in leukaemia), may yield valuable supplementary indications; thus the plasma is golden-yellow in haemolysis, remarkably clear in iron-deficiency anaemia, straw-coloured in pernicious anaemia, cloudy in nephrosis and diabetes owing to increase in lipids and pathological proteins and after ingestion of fats.

	Normal values	Methods and bibliography	Remarks
Surface tension			
16–18° C (serum)	57–58 dyn cm ⁻¹	Cf. for example LOISELEUR, J., <i>Techniques de Laboratoire</i> , Paris, 1947, page 50.	
37° C (serum)	47 dyn cm ⁻¹		
Refractive index			
(fasting, at 20° C)			
(serum)	1.34846–1.35132 (adults)	Using the ABBÉ refractometer. Values from WUHRMANN and WUNDERLY, <i>Die Bluteiweisskörper des Menschen</i> , Basle, 1952.	Can be used as a method for the rapid determination of serum protein content (cf. <i>Zeitschnschriften</i> , 1939). The values given here correspond to a protein content of 6.5–8.2% (adults) and 5.4 to 6.5% (newborn). The accuracy of this method is very largely dependent on the constancy of the concentration of the non-protein bodies, above all that of the lipids and bilirubin. In the case of a large increase in the lipid vectors (α- and β-globulins) the KJELDAHL method is therefore preferable ¹³ .
	1.34575–1.34798 (newborn)		

¹⁾ GILLIGAN and ERNSTENE, *Amer. J. med. Sci.*, **187**, 552, 1934. ²⁾ LUCIA et al., *Amer. J. med. Sci.*, **192**, 179, 1936. ³⁾ GORDON and WARDLEY, *Biochem. J.*, **37**, 393, 1943. ⁴⁾ BENDIN and SNAPPER, *Biochem. Z.*, **235**, 14, 1931. ⁵⁾ HAM and CURTIS, *Medicine*, **17**, 447, 1938. ⁶⁾ THYGESEN, *Acta med. scand.*, Suppl. **84**, 1942. ⁷⁾ KATZ and LEFKOWITZ, *Ergebn. inn. Med. Kinderheilk.*, **33**, 266, 1928. ⁸⁾ WINTROBE, M. M., *Int. Clin.*, **46**, ser., 2, 34, 1936. ⁹⁾ HIRSCHBOECK, J. S., *Blood*, **2**, 578, 1947. ¹⁰⁾ WINTROBE, M. M., *Clinical Hematology*, Philadelphia, 1952. ¹¹⁾ OLBRICH, O., *Fidinh. med. J.*, **55**, 100, 1948. ¹²⁾ WUHRMANN, F., in WUHRMANN and WUNDERLY, *Die Bluteiweisskörper des Menschen*, Basle, 1952. ¹³⁾ MALMROS and BLIN, *Acta med. scand.*, Suppl. **170**, 282, 1946.

		Methods and bibliography	Remarks
Specific conductivity (serum) (at 25°C)	0.01173–0.01229 S × cm ⁻¹ * . . . mean 0.01190 S × cm ⁻¹ *	After SUNDERMAN, F. W., <i>Amer. J. clin. Path.</i> , 15, 219, 1945.	The specific conductivity and the total protein content of the serum enable the total serum bases to be readily calculated.



Nomogram for the determination of total serum bases from specific conductivity and total protein content of serum. After LUFKIN and SUNDERMAN, *Amer. J. clin. Path.*, 16, 118, 1946.

Hydrogen-ion concentration	Arteries (plasma)	Veins (plasma)	Capillaries (plasma)	Methods and bibliography	Remarks
Children (boys and girls)					
Birth to 10 days	–	7.30–7.46 mean 7.38	7.31–7.53 mean 7.42	Values from SINGER and HASTINGS, <i>Acid-Base Data for Human Blood: Normal Standards and Some Physiological Variations</i> , Washington, 1950.	Cf. pages 330 and 331.
1 month to 2 years	–	mean 7.38	–		
6–15 years	7.33–7.47 mean 7.40	7.32–7.44 mean 7.38	–		
Men 16–50 years	7.33–7.45 mean 7.39	7.27–7.43 mean 7.35	7.33–7.45 mean 7.39	GRAIG et al., <i>Fed. Proc.</i> , 10, 301, 1951; indicator or electrometric methods, or calculated from the ratio of carbonate to bicarbonate ions (cf. pages 330 and 331).	
Women 16–50 years	–	7.31–7.43 mean 7.37	7.35–7.47 mean 7.41		
Men over 50	7.32–7.52 mean 7.42	–	7.32–7.46 mean 7.39		
Women over 50	7.34–7.50 mean 7.42	–	–		

* S × cm⁻¹ = Siemens × cm⁻¹ = Ω⁻¹cm⁻¹.

Normal values

(For definition of the normal range, see footnote page 317)

	Normal values	Methods and bibliography	Remarks
Electric charge (per erythrocyte)			
in electrostatic units	0.00734 esu	Value from ABRAMSON and MOYER, <i>J. gen. Physiol.</i> , 19 , 601, 1936.	Calculated from the electrophoretic mobility on the basis of an erythrocyte surface area of 163 μm^2 per cell.
Electrophoretic mobility			
(1) Erythrocytes	$-1.31 \times 10^{-4} \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$..	(1) Phosphate buffer, pH 7.4. Value from ABRAMSON and MOYER, <i>J. gen. Physiol.</i> , 19 , 601, 1936.	
(2) Plasma proteins		(2) Barbitone/barbitone sodium buffer with $\Gamma/2 = 0.1$, pH 8.6, 2°C. Values from ARMSTRONG et al., <i>J. Amer. chem. Soc.</i> , 69 , 416, 1947.	
Albumins	5.7–6.2	} $\times (-10^{-5})$ $\text{cm}^2 \text{ V}^{-1} \text{ s}^{-1}$	
α_1 -Globulins	4.6–5.1		
α_2 -Globulins	3.6–4.1		
β -Globulins	2.5–3.2		
Fibrinogen	1.7–2.3		
γ -Globulins	0.8–1.3		
Specific heat			
in gram calories (plasma)	0.94 cal	Values from MENDLOWITZ, M., <i>Science</i> , 107 , 97, 1948.	
(erythrocytes) ...	0.77 cal		
(whole blood) ..	0.87 cal		
Bleeding time (capillary)			
in seconds	0–450; mean 147 s	According to the method of DUKE, W. W., <i>J. Amer. med. Ass.</i> , 55 , 1185, 1910; make a 3–4 mm deep puncture in the lobe of the ear or finger; remove the drops every 15–30 sec. Values from TOCANTINS, L. M., <i>Med. Clin. N. Amer.</i> , 130 , 1361, 1946.	The bleeding time is primarily a measure of the reaction of the capillaries, since the principal factor controlling bleeding from small skin lesions is the constriction of the small blood vessels which are injured. For blood coagulation scheme, see page 311.
Coagulation time <i>in vitro</i> (in minutes)			
(1) Venous blood } at room temp. {	5 – 8; mean 6.5 min	(1) and (2), method and values from LEE and WHITE, <i>Amer. J. med. Sci.</i> , 145 , 495, 1913. (3) method of LEE and WHITE (<i>loc. cit.</i>), values from TOCANTINS, L. M., <i>Med. Clin. N. Amer.</i> , 30 , 1361, 1946. (4) and (5), method and values from AGGELER and LUCIA, <i>Blood</i> , 1 , 472, 1946.	The coagulation time varies with the method and is dependent on a number of factors: temperature, nature of the surface of the test tube (uncoated, coated with paraffin or silicones), diameter of the test tube (the smaller the diameter the more rapid the coagulation), etc. Precautions must above all be taken that in drawing the blood (capillary) the tissues are not injured (even the slightest pressure should be avoided), or that tissue factors (venous blood) are not introduced into the sample (thromboplastin, etc.), as the test will thereby be invalidated. For this reason venous blood is preferable to capillary. – Even the best determination of coagulation time is only of relative value since it does not reveal which of the numerous factors influencing the coagulation time is responsible for an abnormal value. These factors are normally present in such an excess that it takes a very large reduction to have any effect on the coagulation time (WINTROBE, M. M., <i>Clinical Hematology</i> , Philadelphia, 1952). For blood coagulation scheme, see page 311.
(2) Capillary blood }	2 – 4; mean 3 min		
(3) Venous blood, at 37°C (98.6°F)	7 – 15; mean 11.5 min		
(4) Venous blood, at room temp. .	3.5–14.3; mean 8.9 min		
(5) Venous blood, at 37°C (98.6°F)	4.7–10.4; mean 7.5 min		
Heparin tolerance test¹ (coagulation time in minutes)			
Heparin tolerance test <i>in vitro</i>¹			
Venous, recalcified sodium oxalate blood, room temperature:			
(1) 1 ml blood + 4 μg heparin:	20–28; mean 25 min	(1) Methods and values from DE TAKATS, <i>Angiology</i> , 1 , 317, 1950; (2) and (3), methods and values from WAUGH and RUDDIK, <i>Canad. med. Ass. J.</i> , 50 , 547, 1944; (4) method of SOULIER and LE BOLLOCH, <i>Rev. Hémat.</i> , 5 , 148, 1950, or SOULIER and LE BOLLOCH, <i>Sem. Hôp. Paris</i> , 26 , 3703, 1950, values from SIGG, B., <i>Schweiz. med. Wschr.</i> , 82 , 284, 1952; (5) method and values from SIGG, B., <i>Schweiz. med. Wschr.</i> , 82 , 762, 1952.	Remarks The coagulability of blood can be better judged from the heparin tolerance test than from the prothrombin time (QUICK's method) since the former test indicates any possible hypercoagulability. In contrast to the prothrombin test, in which a number of coagulation factors are eliminated (platelet factor, antihæmophilic globulin, antithrombin and thrombin), the heparin coagulation time (on whole blood) includes all coagulation factors, without their individual rôles being as yet understood. The heparin tolerance test and the prothrombin test do not therefore always correspond. – Heparin coagulation times are not directly comparable and parallel tests with normal subjects are absolutely necessary. (After SOULIER, <i>loc. cit.</i> , and SIGG, <i>loc. cit.</i>)
(2) 1 ml blood + 1.5 μg heparin ² :	19–38; mean 28 min		
(3) 1 ml blood + 3.1 μg heparin ² :	35–60; mean 48 min		
Venous, recalcified potassium and ammonium oxalate ³ plasma, room temperature:			
(4) 0.5 ml plasma + 7.7 μg heparin ² :	8–15 min		
Capillary, recalcified sodium oxalate blood, 37°C (98.6°F)			
(5) 0.15 ml blood + 5.8 μg heparin ² :	8–14; mean 11 min		
Heparin tolerance test <i>in vivo</i>¹			
Venous blood, 37°C (98.6°F)			
(6) 10 min after 10 mg heparin i.v.:	40–90 min		
(7) 10 min after 10 mg heparin i.v.:	5–7 min		

¹ In USA the heparin tolerance test *in vitro* is occasionally referred to as "heparin-retarded coagulation time" and only the test *in vivo* as "heparin tolerance test".² Given in heparin units in the original publication: 1 I.U. = 7.7 μg ; 1 μg = 0.13 I.U. (for international unit, see page 78).³ WINTROBE mixture, cf. Sedimentation rate, page 306.

Normal values

(For definition of the normal range, see footnote page 317)

	Normal values	Methods and bibliography	Remarks	
Blood-clot retraction (syneresis)				
Volume of the separated serum as per cent of the total serum of the sample: (venous blood in paraffin-coated tube of 13 mm dia., after 2 hours at 37° C (98.6° F))	62–94; mean 78.1 vol% . . .	Method of TOCANTINS, L. M., <i>Med. Clin. N. Amer.</i> , 130 , 1361, 1946.		
Time (in minutes)				
(1) 1 drop of blood in castor oil...	20–45; mean 33 min	(1) Method of HIRSCHBOECK, J. S., <i>J. Lab. clin. Med.</i> , 33 , 347, 1948. (2) DIGGS, L. W., in ALBRITTON, E. C., <i>Standard Values in Blood</i> , Philadelphia, 1952.	Values by the methods given are not comparable with those by other methods. The prothrombin time can only be evaluated in comparison with continuous normal controls made in the same laboratory. – The prothrombin time is increased in prothrombin deficiency, inter alia after administration of dicoumarol and its derivatives, in severe injury of the liver parenchyma, especially in acute yellow atrophy of the liver. – For blood coagulation scheme, see the following page. The heparin tolerance test also gives a very good estimate of the coagulability of the blood (see the previous page).	
(2) Venous blood in test tube at room temperature	30–60 min			
Prothrombin time (in seconds)				
at 37° C (98.6° F), venous oxalate blood + calcium chloride				
(1) Thromboplastin* from rabbit brain	11–12 s	(1) Method and values from QUICK, A. J., <i>Amer. J. clin. Path.</i> , 15 , 560, 1945; (2) and (3) method and values from AGGELER and LUCIA, <i>Blood</i> , 1 , 220, 1946; (4) method and values from SHAPIRO et al., <i>J. Lab. clin. Med.</i> , 26 , 723, 1941.		
(2) Thromboplastin* from human brain	10–13; mean 11.5 s			
(3) Thromboplastin* from human brain, plasma 50% (diluted with physiological saline) . . .	13–19; mean 16 s			
(4) Thromboplastin* from rabbit brain, plasma 12.5% (diluted with physiological saline) . . .	34–48; mean 41 s			

Guiding principles for practice (after WUHRMANN, F., in WUHRMANN and WUNDERLY, *Die Bluteiweisskörper des Menschen*, Basle, 1952).

- The prothrombin determination (coagulation time after QUICK) is a very delicate process suitable only for laboratories with special experience and demanding great caution in the interpretation of the results.
- It should be constantly borne in mind that *coagulatory disturbances such as haemophilia* are not necessarily due to prothrombin deficiency (rôle of fibrinogen and other plasma factors, of the blood platelets, of the so-called vascular or capillary factors), and that a lowering of the prothrombin will not necessarily lead automatically to haemophilia.
- Clinically the prothrombin determination is of most importance in the problem of thromboembolism and its treatment with *anticoagulants*, in

which the liver should be kept continuously under observation, particularly in the case of patients with cardiovascular troubles.

- In cases of *diffuse disease of the liver* the prothrombin determination does not fully reflect the hepatic function, although valuable indications as to the general condition may often be obtained; low prothrombin values indicate severe injury of a diffuse nature, particularly such as occurs in acute yellow atrophy of the liver, although a normal value does not necessarily exclude even a severe functional disturbance (QUICK, A. J., *J. Amer. med. Ass.*, **110**, 1658, 1938).
- Within certain limits and above all in the early stages, *vitamin-K loading* can be used successfully as a test for the presence of an *obstructive jaundice*. In the same way a determination of coagulation time is today an indispensable prelude to surgery of the liver or the larger bile ducts.

* Thromboplastin = Thrombokinase.

Osmotic fragility of the erythrocytes

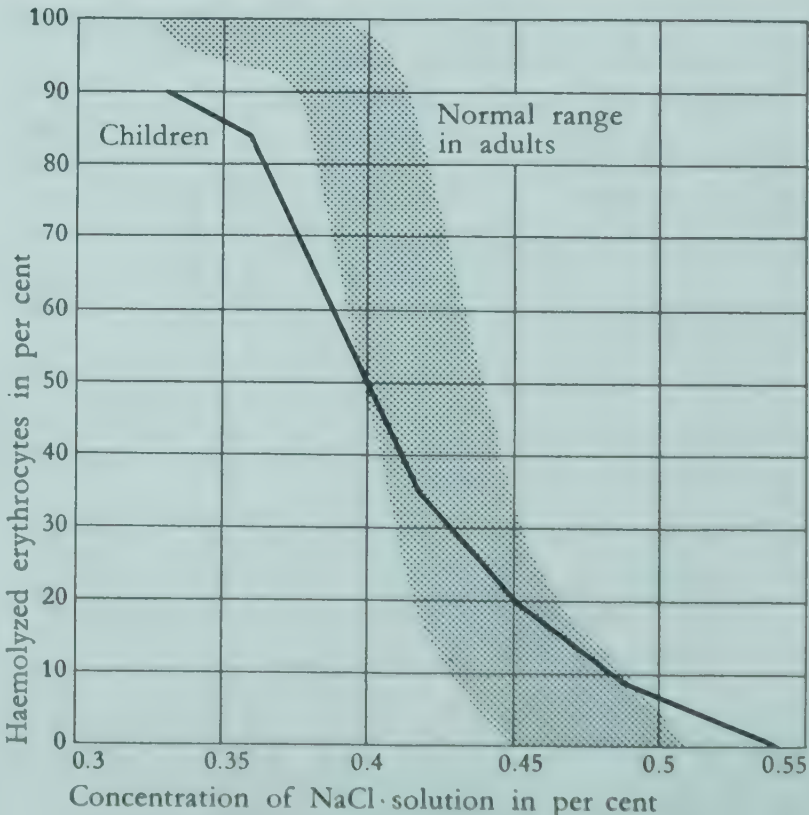
Beginning of haemolysis 0.45–0.39 % NaCl
Complete haemolysis 0.33–0.30 % NaCl
(Method and values after WINTROBE, M. M.⁷⁾

Remarks

The fragility of the erythrocytes is the greater the more globular the shape of the cells^{1,2}. Spherocytes are thus nearer the haemolyzing point while the smaller and thicker normal corpuscles only haemolyze at higher NaCl-concentrations. Some authors regard young erythrocytes, especially reticulocytes, as more resistant to haemolysis^{2,3} while others consider the older erythrocytes as more resistant^{4,5}.

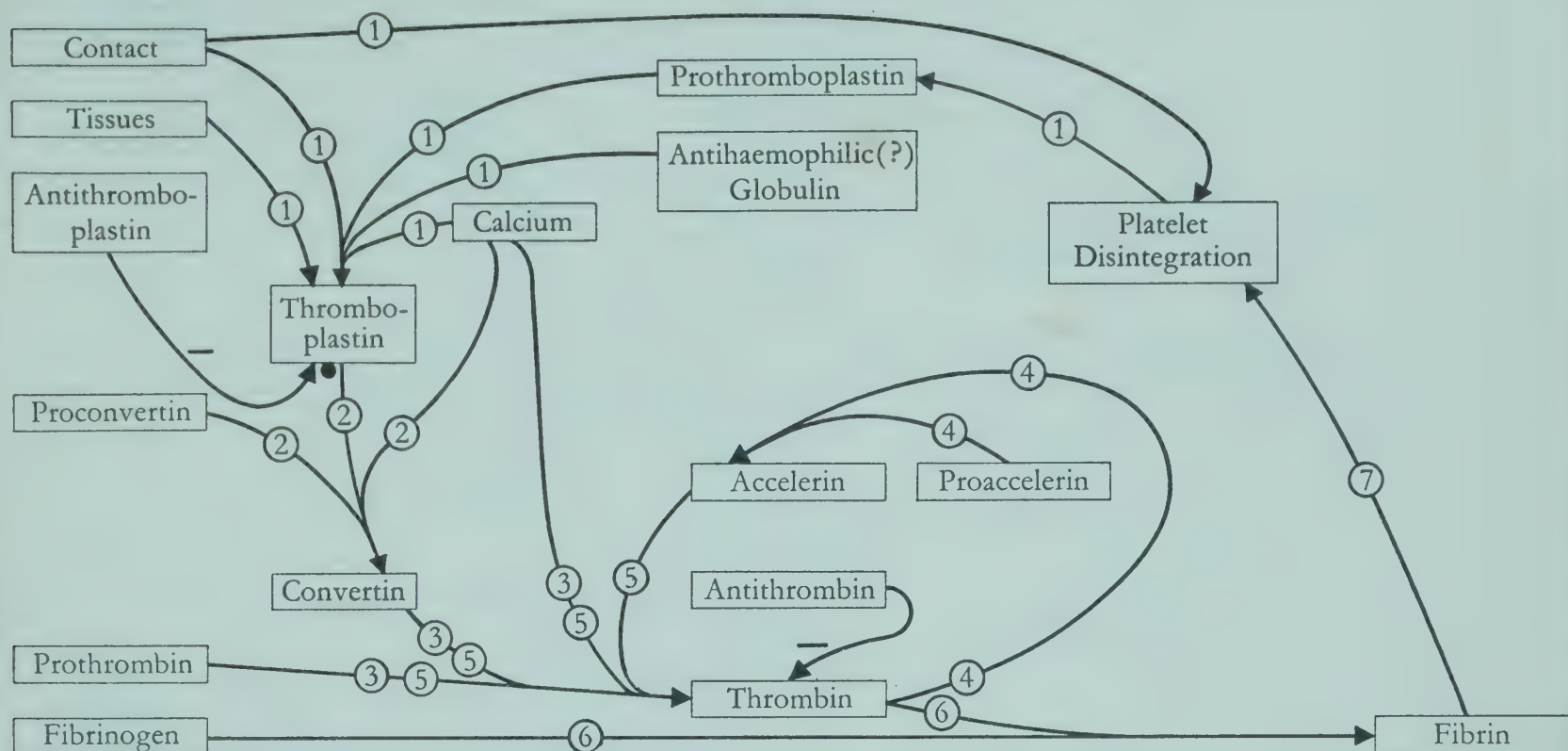
Physiological variations: the osmotic fragility of the erythrocytes in venous blood is greater than that in arterial blood⁶. The erythrocytes of newborn infants are somewhat more fragile than those of adults⁷.

Pathological variations: in congenital haemolytic jaundice the fragility of the erythrocytes is markedly increased. The *opposite* occurs in polycythaemia vera, in “Mediterranean disease” (COOLEY’s or erythroblastic anaemia, in which the resistance may increase up to 0.03 % NaCl), in sickle-cell anaemia and in some cases of hypochromic anaemia.



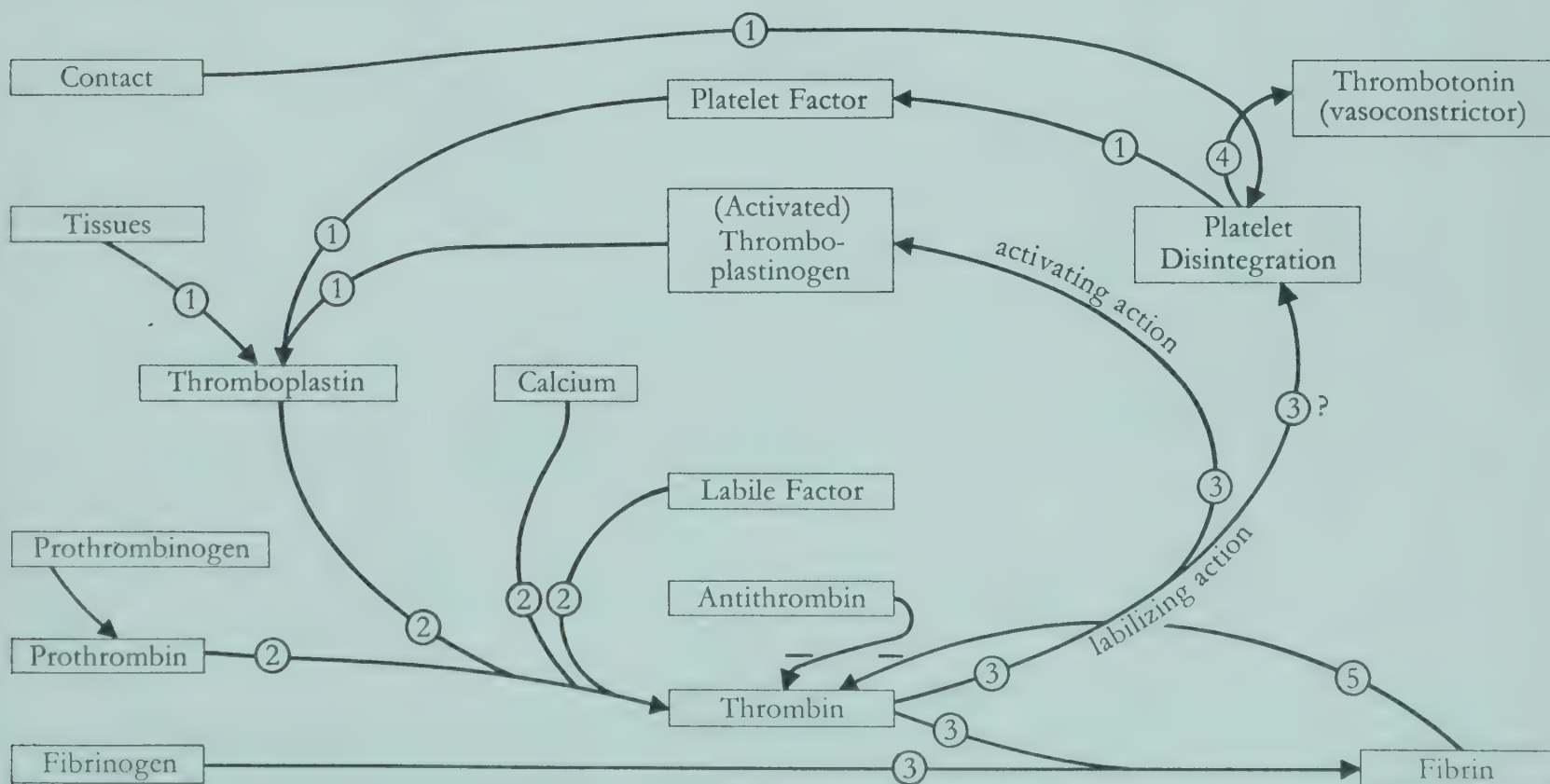
¹⁾ HADEN, R. L., *Amer. J. med. Sci.*, **188**, 441, 1934. ²⁾ DAMESHEK, W., *Blood*, Special Issue, No. 2, 43, 1948. ³⁾ DALAND and WORTHLEY, *J. Lab. clin. Med.*, **20**, 1122, 1935. ⁴⁾ CRUZ et al., *Amer. J. med. Sci.*, **202**, 157, 1941. ⁵⁾ STEWART et al., *J. exp. Med.*, **91**, 147, 1950. ⁶⁾ WHITBY and HYNES, *J. Path. Bact.*, **40**, 219, 1935. ⁷⁾ WINTROBE, M. M., *Clinical Hematology*, Philadelphia, 1952.

Diagram after WHITBY and HYNES⁶.

Blood coagulation theory of P. A. OWREN (1952)¹

Legend:

- ① Tissue injury yields thromboplastin* directly, while contact causes disintegration of platelets and release of prothromboplastin*, which is activated by contact, "antihæmophilic globulin" and calcium to give thromboplastin*.
 - ② Thromboplastin* and proconvertin in the presence of calcium form convertin. An anticonvertin probably exists which opposes the activity of convertin.
 - ③ Convertin together with calcium brings about a minimal conversion of prothrombin to thrombin.
 - ④ This initially formed thrombin starts the accelerator system, i.e. the conversion of proaccelerin to accelerin.
 - ⑤ Accelerin accelerates the conversion of prothrombin to thrombin in the presence of convertin and calcium.
 - ⑥ Thrombin is now in sufficient quantity to convert fibrinogen to fibrin.
- Fibrin provokes the disintegration of the platelets with further release of thromboplastic substances already mentioned.

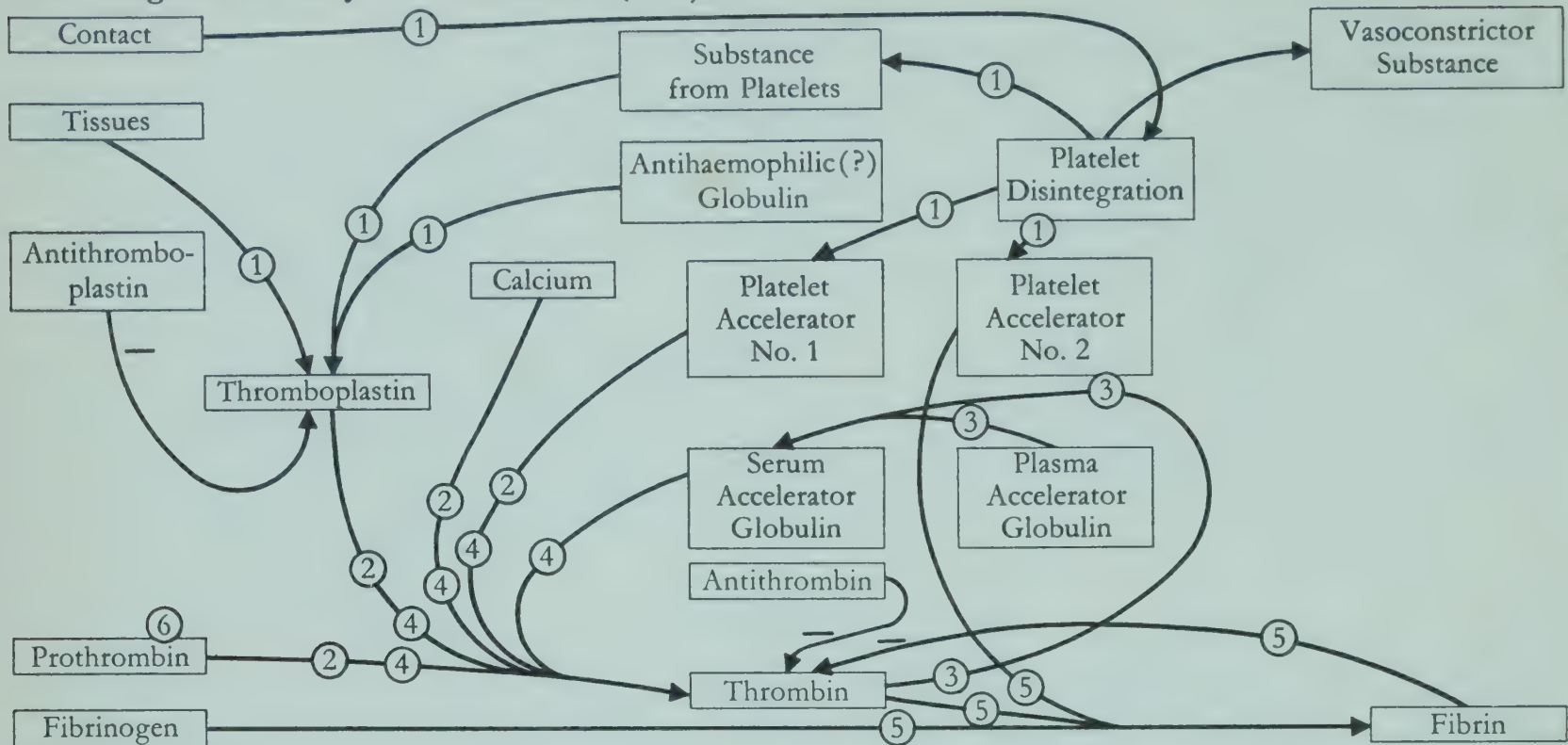
Blood coagulation theory of A. J. QUICK (1952)²

Legend:

- ① Thromboplastin* is (a) released directly by injured tissue and is also (b) formed by the interaction of plasma thromboplastinogen* and a platelet factor, the latter released from disintegrating platelets.
- ② Thromboplastin*, prothrombin, calcium and a labile factor interact stoichiometrically to form thrombin. In human blood part of the prothrombin is in an inactive form, prothrombinogen. On contact with a rough surface it becomes activated.
- ③ The thrombin formed not only converts fibrinogen to fibrin, but activates thromboplastinogen* and thereby probably brings about the lysis of platelets and initiates the chain reaction.
- ④ The platelets also release a vasoconstrictor, thrombotonin, under the labilizing action of thrombin. The resulting local vasoconstriction aids in the hæmostatic process.
- ⑤ The prompt removal of thrombin by fibrin holds in check the autocatalytic reaction mediated through the action of thrombin on platelets and thromboplastinogen*.

* Thromboplastin = Thrombokinase. ¹) OWREN, P. A., in ALBRITTON, E. C., *Standard Values in Blood*, Philadelphia, 1952. ²) QUICK, A. J., *ibid.*, 1952.

Blood coagulation theory of W. H. SEEGERS (1952)¹

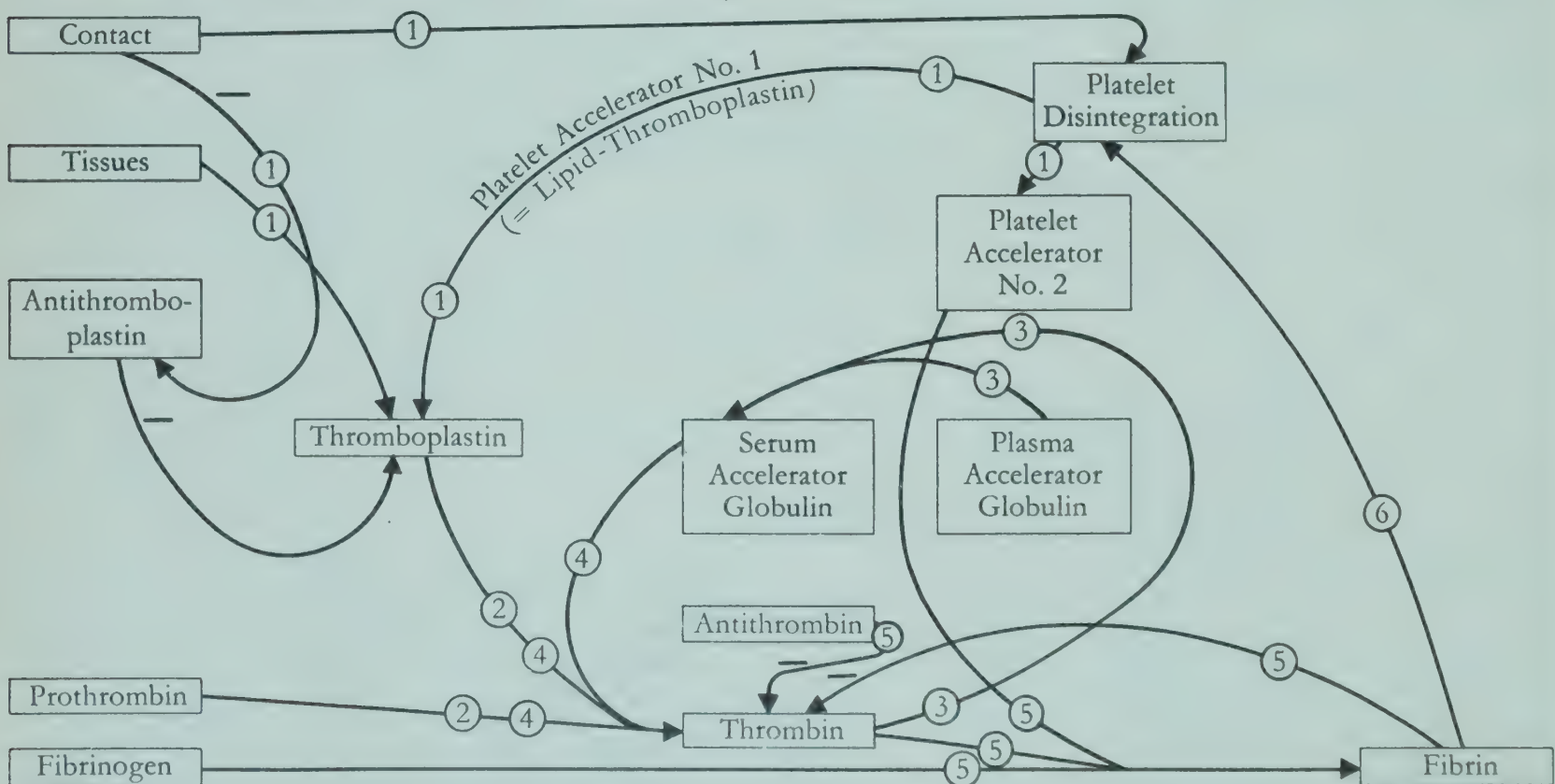


Legend:

- ① Injured tissue yields thromboplastin* directly, while contact causes disintegration of the platelets and the release from them of (a) a substance which reacts with a globulin in the plasma to give thromboplastin*, and (b) two platelet accelerator principles, Nos. 1 and 2.
- ② Thromboplastin* and calcium, together with platelet accelerator No. 1, bring about a minimal conversion of prothrombin to thrombin.
- ③ This initially formed thrombin starts the accelerator system, i.e. the conversion of the proenzyme, plasma Ac-globulin, into the enzyme, serum Ac-globulin.

- ④ Thromboplastin* and calcium, together with serum Ac-globulin and platelet accelerator No. 1, cause accelerated conversion of prothrombin to thrombin.
- ⑤ The now sufficient quantity of thrombin, together with platelet accelerator No. 2, converts fibrinogen to fibrin. Fibrin, by adsorption, inactivates some of the thrombin.
- ⑥ Since purified prothrombin can be activated to thrombin by simply placing it in 2.5% sodium citrate solution, it is believed that prothrombin itself contains all of the necessary material substance for the formation of thrombin. Consequently the activators of prothrombin are catalysts and do not enter into stoichiometric combination with prothrombin to form thrombin.

Blood coagulation theory of L. M. TOCANTINS (1952)²



Legend:

- ① Contact of the blood with certain surfaces (damaged blood-vessel endothelium, glass) initiates the first changes which lead to the inception of clotting: blood platelets agglutinate, adhere to the surface and/or disintegrate, releasing (a) thromboplastin* and (b) fibrinoplastic factor (platelet accelerator No. 2). Some of the thromboplastin* of the blood is offset or neutralized by the antithromboplastin*; some of the antithromboplastin* is itself adsorbed or neutralized at the contacting surface.
- ② Thromboplastin* (from tissues and/or platelets) brings about a minimal conversion of prothrombin to thrombin.

- ③ This initially formed thrombin activates the accelerator system, i.e. the conversion of inactive plasma Ac-globulin to active serum Ac-globulin.
- ④ Thromboplastin* together with serum Ac-globulin causes acceleration of the conversion of prothrombin to thrombin.
- ⑤ Some of the thrombin may be inactivated by antithrombin. The thrombin that escapes such inactivation acts, with the aid of platelet accelerator No. 2, to cause the conversion of fibrinogen to fibrin. Some of the excess thrombin is removed from the plasma by adsorption on fibrin.
- ⑥ Fibrin probably causes further disintegration of platelets.

* Thromboplastin = Thrombokinase. ¹) SEEGERS, W. H., in ALBRITTON, E. C., *Standard Values in Blood*, Philadelphia, 1952. ²) TOCANTINS, L. M., *ibid.*, 1952.

Normal values

(For normal range and standard deviation σ , see footnote page 317)

Adults (plasma)

Legend (table for adults):

* Calculated from mean values in g/100 ml plasma assuming normal specific gravity of plasma (1.026).

** Calculated from mean values in g/100 ml plasma assuming that a normal total protein content of 6.72 g/100 ml plasma = 100%.

*** Calculated from the given mean values in g/100 ml plasma.

† In agreement with LEVER et al., see next page under 4.

The standard deviations of the values from footnotes 4 (a, b, c, d, e, f), 4 (b, c, d, e), 4 (b, c) have been calculated from the formula $\sigma = \sqrt{\sigma_1^2 + \sigma_2^2 + \dots}$

Fraction	Electrophoretic method (TISELIUS ¹)						Salt fractionation method (HOWE ²) with sodium sulphate followed by KJELDAHL ^{6,13} determination					
	% plasma (g/100g plasma) mean*	% total proteins (g/100 g total proteins of plasma) mean**	g/100 g plasma			Values from (footnote)	% plasma (g/100g plasma) mean*	% total proteins (g/100 g total proteins of plasma) mean**	g/100 g plasma			Values from (foot-note)
			Mean	Normal range (mean \pm 2 σ)	Standard deviation				Mean	Normal range (mean \pm 2 σ)	Standard deviation	
Total proteins	6.52	100	6.72	6.02 – 7.42	0.35	Calcul. from 4 (a, b, c, d, e, f)	6.98	100	7.2	6.5 – 7.9	0.35	3
Albumins	3.92	60	4.04†	3.50 – 4.58	0.27	4a	5.04	72.3	5.2	4.7 – 5.7	0.25	3
Globulins	2.27	35	2.34	1.92 – 2.76	0.21	Calcul. from 4 (b, c, d, e)	1.94	27.7	2.0	1.46 – 2.54	0.27	3
α -Globulins	0.77	11.8	0.79	0.654 – 0.856	0.073	Calcul. from 4 (b, c)	–	–	–	–	–	–
α_1 -Globulins ...	0.315	4.6	0.31	0.208 – 0.412	0.051	4b	–	–	–	–	–	–
α_2 -Globulins ...	0.465	7.2	0.48	0.374 – 0.586	0.053	4c	–	–	–	–	–	–
β -Globulins	0.78	12.1	0.81	0.558 – 1.062	0.126	4d	–	–	–	–	–	–
γ -Globulins	0.72	11.1	0.74†	0.438 – 1.042	0.151	4e	–	–	–	–	–	–
Euglobulin	–	–	–	–	–	–	0.194	2.8	0.2	0 – 0.42	0.11	3
Pseudoglobulin I ..	–	–	–	–	–	–	1.26	18.0	1.3	0.84 – 1.76	0.23	3
Pseudoglobulin II ..	–	–	–	–	–	–	0.485	6.9	0.5	0.18 – 0.82	0.16	3
Fibrinogen	0.33	5	0.34	0.222 – 0.458	0.059	4f	Determined gravimetrically					
							0.26	–	0.27	0.17 – 0.37	0.051	5
Ratio albumins : globulins						mean*** 1.73	mean*** 2.6					

Exchangeable albumin pool²⁷: total 259 \pm 40 g; per square meter body surface 232 \pm 34 g

Children (plasma and serum)

Total proteins (in g/100 ml)								Protein fractions (in g/100 ml)					
	Age	KJELDAHL ^{6, 13}		Values from (foot-note)	Refractometric ⁷		Values from (foot-note)	Fraction	Age	Salt fractionation method (HOWE ²) with sodium sulphate followed by KJELDAHL ^{6, 13} determination			
		Mean	Range		Mean	Range				Mean	Normal range (mean \pm 2 σ)	Standard deviation	Values from (foot-note)
Plasma ...	At birth	5.89	5.46–6.31	8				Serum					
Serum	Umbilical blood	6.4	5.3 – 7.7	9	6.04	5.15–7.43	10	Total proteins .	At birth ...	5.52	4.36–6.68	0.58	11
	At birth	5.52	4.36–6.68	11				Albumins	At birth ...	3.73	3.11–4.35	0.31	11
	1–2 days	–	–	–	6.03	5.10–7.02	10	Globulins	At birth ...	1.78	0.88–2.68	0.45	11
	3–4 days	–	–	–	5.89	5.15–6.67	10	Ratio albumins:					
	5–6 days	–	–	–	6.02	5.10–7.01	10	globulins ...	At birth	2.16	1.42–2.90	0.37	11
	7–8 days	–	–	–	5.93	5.10–6.60	10	Total proteins .	5–6 months	6.29	5.63–6.95	0.33	11
	5–6 months .	6.29	5.63–6.95	11				Albumins	5–6 months	4.28	3.52–5.04	0.38	11
	Premat. births.							Globulins	5–6 months	2.01	1.33–2.69	0.34	11
	3–5 days	4.62	3.62–5.36	12				Ratio albumins:					
	8–18 days ...	4.42	3.80–5.02	12				globulins ...	5–6 months	2.14	1.26–3.02	0.44	11

Concentration of sodium sulphate and sulphite required for precipitation of the various protein fractions

Fraction	Sodium sulphate ²		Sodium sulphite ¹⁸	
	mol/litre	g/100 ml	mol/litre	g/100 ml
Fibrinogen	0.76	10.6	0.906	11.4
Euglobulin	1.00	14.2	1.131	14.25
Pseudoglobulin (I.U.)	1.25	17.7	1.355	17.1
Total globulins	1.50	21.5	1.58	19.95

The electrophoretic and sodium sulphate fractions are related as follows: In normal serum the electrophoretic picture is usually unchanged after precipitation of the euglobulins (13.5% sodium sulphate); precipitation of the euglobulin + pseudoglobulin (17.4% sodium sulphate) removes ca. 50% of the α -globulins

and 25% of the β -globulins (no γ -globulins). 21.5% sodium sulphate removes all the γ -globulins, 75% of the β -globulins and 50% of the α -globulins.

Methods of determination²⁵

Total proteins: micro-KJELDAHL^{6,13}, refractometrically⁷, colorimetrically (biuret methods)^{14,15,16}, from the specific gravity of the plasma (cf. page 304), gravimetrically²⁶.

Protein fractions: salt fractionation methods of HOWE², MAJOOR¹⁷, CAMPBELL¹⁸, WOLFSON¹⁶, electrophoretically^{1,26}, by paper electrophoresis¹⁹, fibrin gravimetrically^{20,26} (see also²¹). WOLFSON's rapid micro-method¹⁶ gives values for albumins, α -, β - and γ -globulins which agree well with those obtained electrophoretically.

Albumin turnover rate: with ¹³¹I-tagged albumin (dilution method)²⁷.

¹) TISELIUS, A., *Tr. Faraday Soc.*, **33**, 524, 1937; *Svensk. Kem. Tidskr.*, **50**, 58, 1938; *Kolloid-Z.*, **85**, 129, 1938; *Harvey Lectures*, **35**, 37, 1939–40. ²) HOWE, P. E., *J. biol. Chem.*, **49**, 93, 1921. ³) GUTMAN et al., *J. clin. Invest.*, **20**, 765, 1941 (36 healthy subjects). ⁴) a, b, c, d, e, f: DOLE, V. P., *J. clin. Invest.*, **23**, 708, 1944. ⁵) SMITH et al., *Fed. Proc.*, **10**, 370, 1951 (975 measurements). ⁶) Cf. HILLER, PLAZIN and VAN SLYKE, *J. biol. Chem.*, **176**, 1401, 1948. ⁷) Cf. page 307. ⁸) POMMERENKE (1936), quoted by SUNDERMAN and BOERNER, *Normal Values in Clinical Medicine*, Philadelphia, 1950. ⁹) ANDERSON and OBERST (1936) quoted by SUNDERMAN, *loc. cit.* ¹⁰) DENZER et al. (1939), quoted by SUNDERMAN, *loc. cit.* ¹¹) DARROW and CARY, *J. Pediatr.*, **3**, 573, 1933. ¹²) YOUNG et al. (1941), quoted by SUNDERMAN, *loc. cit.* ¹³) Cf. PREGL, F., *Quantitative Organic Micro-Analysis*, Philadelphia, 1937. ¹⁴) KINGSLEY, G. R., *J. Lab. clin. Med.*, **27**, 840, 1942. ¹⁵) WEICHELBAUM, *Amer. J. clin. Path.*, **10**, 49, 1946. ¹⁶) WOLFSON et al., *Amer. J. clin. Path.*, **18**, 723, 1948. ¹⁷) MAJOOR, C. L. H., *J. biol. Chem.*, **169**, 583, 1947; *Yale, J. biol. Med.*, **18**, 419, 1945–46. ¹⁸) CAMPBELL and HANNA, *J. biol. Chem.*, **119**, 15, 1937. ¹⁹) CRAMER, F., *Papierchromatographie*, 2nd ed., Weinheim, 1953. ²⁰) GRAM, H. C., *Amer. J. med. Sci.*, **168**, 511, 1924. ²¹) MORRISON, P. R., *J. Amer. chem. Soc.*, **69**, 2723, 1947. ²²) Review and description of various methods, cf. WUHRMANN and WUNDERLY, *Die Bluteiweisskörper des Menschen*, Basle, 1952. ²³) LANG, K., in HINSBERG-LANG, *Medizinische Chemie*, Munich, 1951, page 527. ²⁴) STERLING, K., *J. clin. Invest.*, **30**, 1228, 1951.

Plasma protein fractions after COHN^{1,2} (fractional precipitation method³)

Electrophoretic fractions	Fraction according to COHN	Approximate plasma content g/100 ml	Sedimentation constant	Molecular weight	Approximate molecular size in angströms	
					Length	Diameter
Serum albumins	V	3.2	4.6	69,000	150	38
α_1 -Globulins	IV-1	0.2	5.0	200,000	300	50
	IV-4	0.1	4-5	(70,000)
α_2 -Globulins	IV-6	0.1	9.0	(300,000)
β_1 -Globulins	IV-7	0.2	5.5	90,000	190	37
	III-0, III-2	0.2	7.0	(150,000)
	III-0	0.1	20.0	500,000-1,000,000
	III-0	0.2		1,300,000	185	185
β_2 -Globulins	III-1	0.2	7.0	(150,000)
γ -Globulins	II	0.5	7.2	156,000	235	44
	II	0.1	10.0	(300,000)
Fibrinogen	1-2	0.2	9.0	400,000	700	38

A rapid method of plasma fractionation after LEVER et al.⁴, based on COHN's method (see above) for small quantities of blood yields in 3 stages the following 4 fractions (without destruction of the biological activity of the proteins in the fractions):

Fractions according to COHN ³	VI	IV + V	I + III	II
Percentage of total plasma proteins	0.2-3.3; mean 2.2	59.8-71.7; mean 65.6	32.0-15.8; mean 22	9.3-14.0; mean 10.8
Cholesterol content of the fraction as percentage of total cholesterol	not measurable	18.0-33.3; mean 26.6	54.8-83.1; mean 71.4	1.5-6.9; mean 4.0
Phospholipid content of the fraction as percentage of total phospholipids	not measurable	33.0-57.0; mean 46.7	51.0-56.6; mean 52.8	0.8-2.3; mean 1.5
Carbohydrates (hexoses) in mg/100 ml	0.52	11.5	17.6	0.64
Electrophoretic fractions as percentage of the fraction (mean values)	—	Albumins 81.3 α_1 -Globulins 7.8 α_2 -Globulins 4.7 β_1 -Globulins 5.5 β_2 -Globulins 0.2 Fibrinogen 0 γ -Globulins 0	Albumins 0.5 α_1 -Globulins 3.5 α_2 -Globulins 13.5 β_1 -Globulins 49.4 β_2 -Globulins } 26.5 Fibrinogen } γ -Globulins 6.8	Albumins 3.1 α_1 -Globulins 0.1 α_2 -Globulins 0 β_1 -Globulins 0 β_2 -Globulins 3.8 γ -Globulins 93.0
Other components or components contained in the above	Traces of fraction IV + V α_1 -Glycoproteins α_2 -Proteins Other small proteins and peptides Urea Glucose	β_1 -metal-combining protein α_2 -Glycoproteins α_2 -Mucoproteins α_1 -Lipoproteins Iodoproteins Cholinesterase Alkaline phosphatase	β_1 -Lipoproteins β_1 -Lipid-poor euglobulins Caeruloplasmin Isoagglutinins Plasminogen Cold-insoluble proteins Prothrombin	Antibodies

Properties and interactions of plasma-protein components³

Principal protein components					Other protein components				
Protein components	Estimated percentage of plasma proteins	Sedi-mentation constant	Approx. isoelectric point	Specific chemical interaction with or carrier of	Protein components	Estimated percentage of plasma proteins	Sedi-mentation constant	Approx. isoelectric point	Specific chemical interaction with or carrier of
Serum albumins ..	52	4.6	4.9	Fatty acids, dyes, bile salts, drugs and mercury { Carbohydrates and barium Thrombin	Prothrombin	0.1	Calcium and thromboplastin
Mercaptalbumin ..	(34)				Plasminogen	Streptokinase
α_2 -Glycoproteins ..	1.2	9	4.9 }		Hypertensinogen	Renin
α_2 -Mucoproteins ..	0.5	9	4.9 }		Iodoproteins	Thyroxine, iodine
Fibrinogen	4	9	<5.3	Iron and copper	Isoagglutinins	(0.03)	6.3	Incompatible erythrocytes
Cold-insoluble globulin	0.15		<5.3		Complement } components }	0.4	{ Antigen-antibody complex
α_1 -Lipoproteins ...	3	5	5.2 }		Amylase	Starch
β_1 -Lipoproteins ...	5	7	5.4 }		Cholinesterase	0.005	4.5	Cboline esters
β_1 -Lipid-poor euglobulins	{ 2 1	7 20	5.5	{ Antigens Antibodies	Alkaline phosphatase	Phosphate esters
β_1 -Metal-combining protein	3	5.0	5.8		Peptidase	L-Leucylglycyl-glycine
β_2 -Globulins	3	7	6.3		β -Glucuronidase	β -Glucuronides
γ -Globulins	{ 11 —	7 10	6.3 }		Caeruloplasmin	4.4	Copper
Total	86		7.3 }		α_1 -Small acid protein	0.5	2.9	3.0	
					α_1 -Bilirubin globulin	0.05	4.7	Bilirubin
					α_2 -Protein	0.1	2.9	Barium
					β_1 -Protein	0.05	5	

¹) COHN et al., *J. Amer. chem. Soc.*, **68**, 459, 1946. ²) COHN, E. J., *History of Plasma Fractionation*, Boston, 1947. ³) COHN et al., *J. Amer. chem. Soc.*, **72**, 465, 1950. ⁴) LEVER et al., *J. clin. Invest.*, **30**, 99, 1951.

Normal values and remarks

Amino-acid and N- and S-composition of albumin, γ-globulin and fibrinogen¹

	Albumin %	γ-Globulin %	Fibrinogen %
Glycine	1.6	4.2	5.6
Alanine	—	—	3.7
Valine	7.7	9.7	4.1
Leucine	11.0	9.3	7.10
Isoleucine	1.7	2.7	4.8
Proline	5.1	8.1	5.7
Phenylalanine	7.8	4.6	4.6
Cysteine	0.70	0.70	0.41
Cystine	5.58	2.37	2.23
Methionine	1.28	1.06	2.52
Tryptophan	0.19	2.86	3.29
Arginine	6.15	4.80	7.8
Histidine	3.5	2.50	2.6
Lysine	12.3	8.1	9.2
Aspartic acid	10.4	8.8	13.1
Glutamic acid	17.4	11.8	14.5
Serine	3.7	11.4	7.0
Threonine	5.0	8.4	6.10
Tyrosine	4.66	6.75	5.5
Total N	15.95	16.03	16.90
Total S	1.96	1.02	1.26
Amido-N	0.880	1.11	—
Indole-N	0.013	0.20	—
Guanidine-N	1.500	1.16	—
Iminazole-N	0.641	0.45	—
Peptide-N	11.555	12.22	—

Remarks (plasma proteins)

General

Earlier clinical and experimental observations²⁻⁵ indicated that the plasma proteins were for the main part synthesized by the liver. Perfusion experiments with ¹⁴C-lysine on the surviving liver have since confirmed this⁶ (the whole of the albumins and fibrinogen, 80% of the globulins). The synthetic capacity of the liver suffices to replace daily ca. 9% of the liver proteins and ca. 25% of the circulating plasma proteins⁶. Direct measurement of the exchangeable albumin pool with ¹³¹I-tagged albumin (cf. page 313) gives, for example, an albumin turnover rate of 6.7 ± 0.93% per day (17.2 ± 2.7 g per day total or 15.4 ± 2 g per day per m² body surface)⁷. This exclusive synthesis of the albumins (and of the fibrinogen) by the liver together with the partial extra-hepatic synthesis of the globulins provides an explanation of the inverted albumin/globulin ratio occurring in advanced cirrhosis of the liver with clinical signs of portal obstruction⁶.

The plasma-protein fractions (albumins, globulins, fibrinogen) bear a close relationship to one another, expressed by the following formula⁸:

$$K = A^{0.62} \times G^{0.328} \times F^{0.052}$$

or $\log K = 0.62 \log A + 0.328 \log G + 0.052 \log F$

where *A*, *G* and *F* are respectively the albumin, globulin and fibrinogen contents and *K* is a constant. 80 TISELIUS diagrams (electrophoresis)⁸ on healthy subjects between the ages 20–45 have given *K* = 0.442 (± 0.002 range of physiological variation). Between the ages 0–45 and 70–95 the corresponding values for *K* are 0.441 (± 0.005) and 0.435 respectively. The value of 0.442 (+) for the ages 20–45 represents a maximum which is never exceeded.

A change in the content of any fraction results in a lowering of this maximum⁸. This fact justifies the assumption of a central regulation of the plasma-protein picture in which the controlling variable is possibly the colloid-osmotic pressure⁹. The albumins can be regarded as the principal factor used by the organism in effecting this regulation; pathologically, a relative diminution in their content may be observed but never a relative increase¹⁰.

Total protein content

The total protein content can only be expressed exactly in terms of the total plasma volume, somewhat less exactly in terms of the haematocrit value, since an increase in the blood-plasma concentration can, effectively, be due to a thickening or thinning of the blood, or conversely an abnormal protein content can be masked by such changes. In practice it is sufficient to determine the haemoglobin content and the erythrocyte count¹⁰. In health the total protein concentration is rather variable, so that only changes of considerable magnitude have any clinical significance. *The total protein content* is increased through desalination in cholera and other diseases with severe diarrhoea, and after severe vomiting (albumins and globulins increased in proportion); also in many infectious diseases as well as in plasma cell myeloma (increase mainly in globulins).

The total protein content is diminished in kidney diseases, particularly nephrosis, in undernourishment (nutritional oedema), in some cases of diabetes (in all these cases it is principally the albumin

¹) After BRAND, E., *Ann. N. Y. Acad. Sci.*, **47**, 187, 1946; completed after TRISTRAM, G. R., *Advanc. Protein Chem.*, **5**, 142, 1949. ²) MADDEN and WHIPPLE, *Physiol. Rev.*, **20**, 194, 1940. ³) WHIPPLE and MADDEN, *Medicine*, **23**, 215, 1944. ⁴) JANSSEN, L. W., *Electrophoretic Studies on Serum Proteins*, Amsterdam, 1951. ⁵) WHIPPLE, G. H., *Amer. J. Physiol.*, **33**, 50, 1941. ⁶) MILLER et al., *J. exp. Med.*, **94**, 431, 1951. ⁷) STERLING, K., *J. clin. Invest.*, **30**, 1228, 1951. ⁸) ECKEN and FRACKLTON, *Fed. Proc.*, **10**, 353, 1951. ⁹) WUNDERLY and WUHRMANN, *Gastroenterologia*, **69**, 121, 1944. ¹⁰) WUHRMANN and WUNDERLY, *Die Blutkreislauffunktion des Menschen*, Basle, 1952.

Total protein content (continued)

content which is lowered), in wasting diseases such as carcinoma and tuberculosis. – A sudden fall in plasma proteins, particularly the albumins, follows operations (irrespective of the type of operation and subsequent nursing). This is soon followed by an increase in the globulins up to and beyond the preoperative level¹⁹ (cf. also Blood volume and Blood chlorides, page 326).

Guiding principles in practice¹

1. The easily determined total protein content of serum or plasma is generally of little clinical importance in acute diseases or those of short duration.
2. Only variations of considerable magnitude have any clinical value, and then only when these marked quantitative changes are accompanied by qualitative changes.
3. Of particular clinical importance is the overall diminution of proteins in blood in chronic disease, especially in wasting diseases such as carcinoma and tuberculosis, also in many chronic liver diseases, particularly in cirrhosis of the liver and chronic inanition.
4. The most marked hypoproteinaemia is observed in the nephrotic syndrome.
5. The most marked hyperproteinaemia, occasionally up to double the normal value, occurs mainly in cases of plasma cell myeloma.
6. The total protein value itself is largely independent of changes in the sedimentation rate, the various turbidity and flocculation reactions, the coagulation threshold and nephelogram; a close relation exists only in the case of extreme variations in protein content accompanied by qualitative changes.
7. In the case of marked changes in total protein content the mineral metabolism, particularly the serum calcium level, should be watched (see page 327).
8. In practice, repeated determination of the haemoglobin content and the erythrocyte count, in place of the haematocrit value, provides a sufficient indication of any possible thinning or thickening of the blood under test.

The plasma protein fractions

(Cf. also the general remarks on the previous page)

The definition of the three main fractions (albumins, globulins, fibrinogen) follows from their separation by the salt fractionation method, although this method does not separate them so sharply as the electrophoretic method, particularly when pathological changes have occurred (for relations between the fractions yielded by the two methods, see page 313). The more recent fractionation methods of COHN et al.^{2,3,4} and LEVER et al.⁵ (see page 314) give sharp fractionation but are too lengthy for routine testing. In spite of their inaccuracy (particularly in the case of pathological changes) the conventional salt fractionation methods, e.g. HOWE's sodium sulphate method²², must therefore be used in practice; in many cases they provide sufficient indication of the clinically significant changes in the plasma protein spectrum, particularly of increases in globulins (mention should also be made of WOLFSON's method⁶).

An increase in globulins and a decrease in albumins is observed *physiologically* in pregnancy (see page 273) and stress (see page 185), and *pathologically* in a great variety of diseases, from simple inflammations to pathologically irreversible destruction of organs, from disturbances of the internal secretions to malignant tumours^{7,8}. As a result of this fluctuation (which is always in the same direction, inasmuch as the albumins suffer a relative decrease but never an increase) the albumin/globulin ratio loses much of its clinical significance; it is clear that in spite of a "normal" value for the ratio considerable pathological changes in the protein spectrum can exist. In practice therefore the rapid and simple blood sedimentation, flocculation and turbidity tests provide much more information.

The magnitudes, concentrations and interactions of the various plasma protein fractions and their components, as well as their biological significance, have been dealt with on the previous pages. In conclusion follows a summary of the principal data:

1. Albumins. The finely-dispersed albumins are primarily responsible for the total plasma volume (see page 305) and for the colloid-osmotic pressure (see page 305). As a result of their relatively small molecular dimensions they possess a high specific surface and are thus capable of acting as carriers of a great variety of substances. *Their content is lowered in general in all pathological conditions.*

2. Globulins. The more coarsely dispersed globulins separate in electrophoresis into a large number of sub-fractions the functions of which vary extremely widely. The α - and β -lipoglobulins, carriers of ca. 75% of the plasma lipids⁹, are increased in all diseases in which the blood lipid content is increased. The γ -globulins, carriers of antibodies, are increased in all infectious diseases and in other conditions in which immunization processes are set in motion. This is the reason for the almost *stereotyped increase of the globulin fraction in practically all diseases*. (Cf. also the increase in pregnancy, page 273.)

In the case of the lipoproteins a positive correlation has been observed¹⁰⁻¹⁶ between age, arteriosclerosis and the content of the Sf_{12-100} -lipoproteins (so designated from their separation by ultracentrifuging) although no explanation of cause and effect has yet been found.

3. Fibrinogen. The fibrinogen is best determined gravimetrically by precipitation as fibrin, since salt fractionation simultaneously precipitates other coarsely dispersed proteins, particularly in pathological conditions, with the result that these are determined as fibrin. Extensive tests¹⁷ (975 tests on 333 individuals) have shown that the *fibrinogen content* is 2–4 times increased 3–7 days after the start of an acute bacterial lung infection, 4–5 days after operations, 5 days after the start of anticoagulant therapy using dicumarol, in acute pancreatitis, in the case of untreated malignant tumours, 3–4 days after radiological treatment. In *virus infections* the fibrinogen content begins to *fall* in the second week and remains below the normal level for up to 7 months. *Fibrinopenia* is usually observed in injury to the liver parenchyma (particularly in acute yellow atrophy of the liver), in hepatic disturbances following extensive burns, in leukaemia, congested liver, obstructive cirrhosis, severe cardiac insufficiency¹⁸. Constitutional afibrinogen-aemia is rare¹, as is also constitutional fibrinopenia^{18,19} and (acquired) fibrinasthenia^{20,21} (functionally defective fibrinogen). On fibrinogen and sedimentation, see page 307).

¹) WUHRMANN and WUNDERLY, *Die Bluteiweisskörper des Menschen*, Basle, 1952. ²) COHN et al., *J. Amer. chem. Soc.*, **68**, 459, 1946. ³) COHN, E. J., *History of Plasma Fractionation*, Boston, 1947. ⁴) COHN et al., *J. Amer. chem. Soc.*, **72**, 465, 1950. ⁵) LEVER et al., *J. clin. Invest.*, **30**, 99, 1951. ⁶) WOLFSON et al., *Amer. J. clin. Path.*, **18**, 723, 1948. ⁷) WUNDERLY and WUHRMANN, *Gastroenterologia*, **69**, 121, 1944. ⁸) LEINWAND, I., *J. Lab. clin. Med.*, **37**, 532, 1951. ⁹) ONCLEY et al., *J. Amer. chem. Soc.*, **72**, 458, 1950. ¹⁰) GOFMAN et al., *Science*, **111**, 166, 1950. ¹¹) GOFMAN et al., *Circulation*, **2**, 161, 1950. ¹²) GOFMAN et al., *J. Geront.*, **6**, 105, 1951. ¹³) LINDGREN et al., *J. Phys. Colloid. Chem.*, **55**, 80, 1951. ¹⁴) JONES et al., *Amer. J. Med.*, **11**, 358, 1951. ¹⁵) GOFMAN et al., *Circulation*, **5**, 119, 1952. ¹⁶) GOFMAN, W. J., *Bull. N. Y. Acad. Med.*, **28**, 279, 1952. ¹⁷) SMITH et al., *Fed. Proc.*, **10**, 370, 1951. ¹⁸) RISACK, E., *Z. klin. Med.*, **128**, 615, 1935. ¹⁹) GLANZMANN et al., *Schweiz. med. Wschr.*, **51**, 1243, 1940. ²⁰) FANCONI, G., *ibid.*, **11**, 255, 1941. ²¹) FANCONI, G., *ibid.*, **35**, 791, 1946. ²²) HOWE, P. E., *J. biol. Chem.*, **49**, 93, 1921. ²³) WILKINSON et al., *Lancet*, **1**, 315, 1951.

Normal values in mg/100 ml, unless otherwise stated

(For definition of the normal range, see footnote)

	Whole blood	Plasma or serum	Methods	Remarks
Nitrogen distribution				
Total N (chemically combined) (For nitrogen as N ₂ , see Blood gases, page 331)	2.6–4.3 g/100 ml	1.1–1.4 g/100 ml	KJELDAHL	Whole blood: mean usually 3%. Protein-N is 99% of total N (96% in plasma or serum). For N-increase and -decrease, see under Proteins.
Total protein-N	2.5–4.3 g/100 ml	1.0–1.4 g/100 ml	KJELDAHL	

Non-protein nitrogen

	Whole blood		Corpuscles		Plasma or serum	
	Normal range	Mean	Normal range	Mean	Normal range	Mean
Total	28–39	32	38–55	44	22–29	25
Urea-N	8.9–15.2	12	8–13	10	9.6–17.6	12
Non-urea-N	16–26	20	25–45	33	6–18	12
Amino-acid-N	4.6–6.8	5.6	6.5–9.6	7.4	3.4–5.0	4.4
Creatine-N	1.0–1.6	1.3	1.9–3.2	2.6	–	–
Creatinine-N	0.4–0.6	0.5	–	–	0.4–0.5	0.4
Uric acid-N	0.3–1.3	0.7	–	–	0.7–1.3	1.3
Glutathione-N	4.4–4.8	4.6	9.5–10.5	10.0	–	–
Nucleotide-N	4.4–7.4	5.8	10–16	13	–	–
Ergothionine-N	0.3–6.3	3.3 σ 1.5	1–11.8	6.4 σ 2.7	–	–
Ammonia-N	0.1–0.2	–	–	–	0.1–0.2	–

Non-protein-N (serum): increased in renal insufficiency, also in extrarenal disturbances such as hypochloraemia, ADDISON's disease, etc.

Cf. remarks under Urea, below.

Serum non-protein-N is made up of nitrogen of urea, free amino-acids, creatine, creatinine, guanidino-acetic acid, purine derivatives, indican, phenols, bilirubin, urobilin, choline, histamine, glutathione, etc. (cf. the following pages).

Non-protein-N components

Urea

(3) Men and women as one group	25.6	19–32.5	–	26.8	13.8–39.8	6.5
(1) Men	–	–	–	27.1	18.1–36.1	4.5
(2) Women	–	–	–	26.4	10.2–42.6	8.1

Urea level in relation to protein intake (young males)

(4) 0.5 g protein	per kg body weight	–	–	19.3	13.5–25.1	2.9
(4) 1.5 g protein	per day	–	–	38.6	24.4–52.8	7.1
(4) 2.0 g protein	per day	–	–	45.5	31.3–59.7	7.2

(Urease): GENTZKOW, C. J., *J. biol. Chem.*, **143**, 531, 1942; OWINGS and MANDEL, *Proc. Soc. exp. Biol.*, **78**, 364, 1951. Another (simple) method: KIBRIK and SKUPP, *Proc. Soc. exp. Biol.*, **73**, 432, 1950. Values (1), (2) from CRAMER and WINNICK, *J. biol. Chem.*, **150**, 259, 1943; values (3) (plasma) calculated from (1) and (3); (4) ADDIS et al., *J. clin. Invest.*, **26**, 869, 1947.

Physiologically, the urea level increases with increased protein intake, as shown by the adjacent values.

Free amino-acids (total) (non-protein amino-acids)

Alanine	4.0	2.8–5.2	–	3.97	2.57–5.37	0.7
Arginine	1.0	0.6–1.7	–	2.24	1.10–3.58	0.62
Aspartic acid	–	–	–	–	0.9–1.2	–
Citrulline	–	–	–	0.5	0.38–0.59	–
Cystine	0.9	0.6–1.2	–	1.4	0.8–2.0	–
Glutamine	–	–	–	5.78	2.68–8.88	1.55
Glutamic acid	–	–	–	3.41	0.63–6.19	1.39
Glycine (glycocoll)	–	1.8–2.5	–	1.77	1.25–2.29	0.26
Histidine	1.3	0.9–1.7	–	1.42	1.06–1.78	0.18
Isoleucine	1.3	0.9–1.5	–	1.60	0.98–2.22	0.31
Leucine	1.7	1.4–2.0	–	1.91	1.23–2.59	0.34
Lysine	2.2	1.3–3.0	–	2.95	2.11–3.79	0.42
Methionine	0.5	0.4–0.6	–	0.85	0.46–1.48	–
Phenylalanine	1.0	0.8–1.2	–	1.38	0.74–1.92	0.32
Proline	–	–	–	–	2.4–2.7	–
Threonine	1.6	1.3–2.0	–	2.02	1.12–2.92	0.45
Tryptophan	0.7	0.5–1.0	–	1.08	0.66–1.50	0.21
Tyrosine	1.1	0.8–1.4	–	1.48	0.74–2.22	0.37
Valine	2.4	2.0–2.9	–	2.83	2.15–3.51	0.34

Microbiological methods: SCHIYSON et al., *J. Lab. clin. Med.*, **35**, 640, 1950. Values are from a summary by KREBS, H. A., *Ann. Rev. Biochem.*, **9**, 417, 1950; completed after GUTMAN and ALEXANDER, *J. biol. Chem.*, **168**, 527, 1947; HIER and BERGHEIM, *ibid.*, **163**, 129, 1946; STEELE et al., *J. Nutr.*, **40**, 145, 1950; JOHNSON and BERGHEIM, *J. biol. Chem.*, **188**, 883, 1951; HIER, S. W., *ibid.*, **171**, 813, 1947; DUNN et al., *ibid.*, **157**, 387, 1945; HENDERSON et al., *ibid.*, **177**, 815, 1949.

Cf. Urea and non-protein-N. – Apart from the amino-acids listed, serine and hydroxyproline are thought to be present since their existence in animal sera has been demonstrated. The amino-acid level rises sharply under corticotropin (BERGENSTRAHL et al., *Proceedings of the Second Clinical ACTH Conference*, Vol. I, 250, 1951).

Non-protein-N and corticotropin (or hydrocortisone or cortisone) therapy. As a result of the antianabolic action of corticotropin, hydrocortisone and the similarly acting cortisone the blood level of all non-protein-N components is as a rule slightly increased in therapy with these hormones. This applies particularly to the free amino-acids.

The normal range: The limits of the normal range are strictly defined by the formula mean \pm 2 \times standard deviation σ (see page 32). The normal range thus calculated is indicated in these tables by bold figures for the mean and italic figures for the standard deviation. When not so indicated the range must be regarded as purely arbitrary.

Normal values in mg/100 ml, unless otherwise stated
(For definition of the normal range, see footnote page 317)

Non-protein-N components (continued)

Creatine

	Whole blood			Plasma or serum			Methods and bibliography	Remarks
	Mean	Normal range (Mean ± 2σ)	Standard deviation σ	Mean	Normal range (Mean ± 2σ)	Standard deviation σ		
(1) Men and women as one group	3.9	2.9–4.9	–	1.07	0.76–1.28	–	(1) after ALLINSON, M. J. C., <i>J. biol. Chem.</i> , 157 , 169, 1945; (2) after TIERNEY and PETERS, <i>J. clin. Invest.</i> , 22 , 595, 1943; and PETERS, H. J., <i>J. biol. Chem.</i> , 146 , 179, 1942.	Cf. Urea and non-protein-N. – ALLINSON's method depends on the use of a creatine-destroying enzyme, TIERNEY and PETERS' is photoelectric.
(as creatinine)								
(1) Men and women as one group	–	–	–	0.42	0.28–0.62	–		
(2) Men	–	–	–	–	0.17–0.50	–		
(2) Women	–	–	–	–	0.35–0.93	–		

Creatinine

Men and women as one group	1.3	1.2–1.5	–	–	–	–	<i>Serum:</i> range after CAMARA, A., <i>J. Lab. clin. Med.</i> , 37 , 743, 1951; mean after ADDIS et al., <i>J. clin. Invest.</i> , 30 , 206, 1951. For errors due to chromogens in JAFFÉ's method, see LAUSON, H. R., <i>J. appl. Physiol.</i> , 4 , 227, 1951.	The creatinine level in blood is relatively constant and does not vary with the nutrient protein intake except when in large amounts in the form of meat.
Men	–	–	–	1.03	0.95–1.29	–		
Women	–	–	–	0.79	0.77–0.98	–		

Guanidinoacetic acid

	–	–	–	0.26	0.24–0.28	–	Values after HOBERMAN, H. D., <i>J. biol. Chem.</i> , 167 , 721, 1947; and LEVEDAHL and SAMUELS, <i>ibid.</i> , 176 , 327, 1948.	
--	---	---	---	------	-----------	---	------------------------------------------------------------------------------------------------------------------------------------------------	--

Methylguanidine

	0.25	0.2–0.3	–	–	–	–	Values after PFIFFNER and MYERS, <i>J. biol. Chem.</i> , 87 , 345, 1930.	
--	------	---------	---	---	---	---	---------------------------------------------------------------------------------	--

Purine derivatives

Nucleotides	41	31–52	–	–	–	–	JACKSON, H., <i>J. biol. Chem.</i> , 57 , 121, 1923.	
-------------	----	-------	---	---	---	---	-------------------------------------------------------------	--

Pyridine nucleotides (as DPN)	3.6	2.6–4.6 (erythrocytes)	–	0.07	0.02–0.12	–	RAPOPORT and GUEST, <i>J. biol. Chem.</i> , 138 , 269, 1941.	DPN = diphosphonucleotide, TPN = triphosphonucleotide (cf. page 218). The ratio DPN:TPN in erythrocytes is estimated at 8:1.
	7.7	6.1–9.3	–					

Ribonucleic acid

	–	–	–	4.9	3.9–5.9	–	MANDEL and METAIS, <i>C. R. Soc. Biol.</i> , 142 , 241, 1948.	
--	---	---	---	-----	---------	---	----------------------------------------------------------------------	--

Desoxyribonucleic acid

	–	–	–	0.8	0–1.6	–	MANDEL and METAIS, <i>loc. cit.</i>	
--	---	---	---	-----	-------	---	-------------------------------------	--

Adenosine triphosphate (ATP)

Men	46	38–54	–	–	–	–	BUELL, M. V., <i>J. biol. Chem.</i> , 108 , 273, 1935.	
Women	39	30–48	–	–	–	–		

Adenosine + adenylic acid (as adenosine)

	–	–	–	1.09	0.32–1.86	0.385	GREEN et al., <i>Clin. Sci.</i> , 8 , 65, 1949.	
--	---	---	---	------	-----------	-------	--------------------------------------------------------	--

Allantoin

	–	–	–	–	0.3–0.6	–	Values after ARCHIBALD, R. M., <i>J. biol. Chem.</i> , 156 , 121, 1944.	
--	---	---	---	---	---------	---	--------------------------------------------------------------------------------	--

Uric acid

	2.0	1.0–3.0	–	4.0	2.9–6.9	–	Serum values after BEN-SELEY et al., <i>J. Lab. clin. Med.</i> , 32 , 1382, 1947.	Cf. Urea and non-protein-N. – In gout the value increases up to 18 mg. For a new method of determination, see BIDMEAD, D. S., <i>J. clin. Path.</i> , 4 , 370, 1951.
--	-----	---------	---	-----	---------	---	------------------------------------------------------------------------------------------	-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Indican

	–	–	–	–	0.026–0.085	–	Values after TOWNSEND, S. R., <i>J. Lab. clin. Med.</i> , 23 , 809, 1938.	Increased in obstipation and renal insufficiency. In uraemia the phenol value always exceeds 2.0 mg/100 ml (GABERMAN et al., <i>J. Lab. clin. Med.</i> , 37 , 544, 1951).
--	---	---	---	---	-------------	---	----------------------------------------------------------------------------------	----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Phenols

	–	2–8	–	–	1–2	–	Values after STOUGHTON, <i>J. biol. Chem.</i> , 115 , 293, 1936.
--	---	-----	---	---	-----	---	-------------------------------------------------------------------------

Choline (free, adults)

	–	–	–	–	0.2–2	–	Values after APPLETON et al., <i>Fed. Proc.</i> , 10 , 157, 1951.	In some individuals constant over long periods. In disease, values are normal, except in kidney diseases, when the value lies on or above the upper limit of the normal range. When the level in blood is normal no choline appears in the urine. Choline injected intravenously is eliminated inside one hour (APPLETON, <i>loc. cit.</i>).
--	---	---	---	---	-------	---	--------------------------------------------------------------------------	-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Acetylcholine

(Healthy subjects)	–	–	–	0.00128	0–0.00368	0.0012	Values after SCUDAMORE, H. H., <i>J. Lab. clin. Med.</i> , 37 , 860, 1951.	Cf. Blood cholinesterase, page 325. The ratio of acetylcholine to choline on the erythrocyte surface is 300:1 (after MARQUARD and HIRSCH, <i>Hoppe-Seyl. Z. physiol. Chem.</i> , 289 , 102, 1952).
(Asthmatics)	–	–	–	0.00397	0.00109–0.00541	0.00144		

Normal values in mg/100 ml, unless otherwise stated
(For definition of the normal range, see footnote page 317)

Non-protein-N
components
(concluded)

	Whole blood			Plasma or serum			Methods and bibliography	Remarks
	Mean	Normal range (Mean \pm 2 σ)	Standard deviation σ	Mean	Normal range (Mean \pm 2 σ)	Standard deviation σ		
Histamine	—	—	—	—	0.002–0.008	—	Values after CODE, C. F., <i>Physiol. Rev.</i> , 32 , 47, 1952, in agreement with ROSE, R., <i>Recent Progr. Hormone Res.</i> , 7 , 375, 1952.	The histamine is probably contained in the polymorphonuclear leucocytes, whence the greatly increased blood histamine content in leukaemia (VALENTINE and LAWRENCE, <i>Amer. J. med. Sci.</i> , 216 , 619, 1948), but definitely not in the eosinophils (HERBERT et al., <i>J. Allergy</i> , 21 , 12, 1950). Cf. ROSE, <i>loc. cit.</i>
Glutathione	35.4	26.9–41.4	—	0	0	—	CAREN and CARNE, <i>Amer. J. med. Sci.</i> , 221 , 307, 1951.	See “Reducing substances”, page 320. Increased in diabetes mellitus (unaffected by insulin); lowered both in healthy and diabetic subjects under corticotropin, hydrocortisone or cortisone therapy.
Ergothioneine	9.6	8.96–10.24	0.32	0	0	—	FRASER, R. S., <i>J. Lab. clin. Med.</i> , 37 , 199, 1951 (94 tests, average age 29½ years).	Significantly lowered only in hypothyreosis, increased in acute appendicitis, anaemia, coronary sclerosis and circulatory diseases, nephrosis and nephritis, dermatitis, fractures, non-tuberculous lung infections, acute infections of the nasopharynx, cholecystitis and cholelithiasis (FRASER, <i>loc. cit.</i>).
Bilirubin								
total (indirect-reacting)*	—	—	—	0.5	0–1.1	0.3	By means of the VAN DEN BERGH diazo-reaction, VAN DEN BERGH, A. A. H., <i>Der Gallenfarbstoff im Blute</i> , Leipzig, 1918. Values in agreement with DUCCI ³ and WATSON ¹¹ (for bibliography, see the following page).	Cf. remarks below.
direct-reacting*	—	—	—	—	max. 0.25	—		

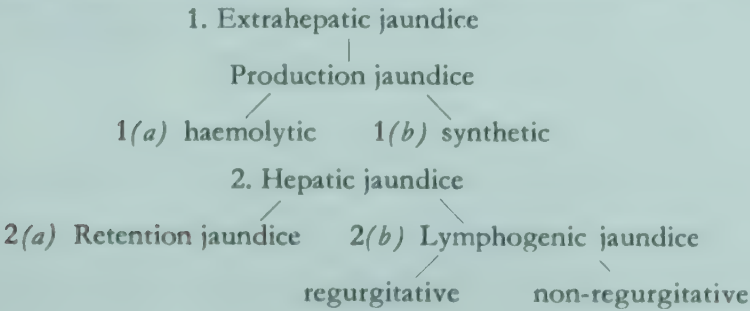
* VAN DEN BERGH reaction

Remarks on bilirubin^{1–13}

Recent investigations have led to a revision of the previously accepted theories regarding bilirubin. The bilirubin of the organism is not, as generally regarded in the past, exclusively a product of the blood regeneration processes. As demonstrated by radiobiological tests with labelled amino-acids, it is normally ca. 15% a product of the haemoglobin synthesis and ca. 85% a product of the breakdown of erythrocytes. In pathological conditions the proportion formed from haemoglobin synthesis can rise to 50%.

In jaundice it is first of all necessary to distinguish between *extrahepatic* and *hepatic* jaundice. *Extrahepatic jaundice* is a result of overproduction of bilirubin (*production jaundice*), whether due to an abnormally high haemoglobin synthesis (*synthetic production jaundice*) or to an abnormally high erythrocyte breakdown (*haemolytic production jaundice*). *Hepatic jaundice* can be due either to diminished excretory capacity of the liver cells (*retention jaundice*) or to the passage of bile into the lymph ducts (*lymphogenic jaundice*), the latter as a result either of regurgitation from ruptured bile ducts (*regurgitative jaundice*) or of some unknown secretory process (*non-regurgitative jaundice*). The latter must be the case, for example, in the early stages of an obstruction jaundice since the pressure in the bile ducts in a rapidly developing jaundice is initially so low that a rupture of the bile capillaries is hardly to be expected.

These distinctions can be expressed diagrammatically thus:



Non-haemolytic hereditary jaundice is probably a synthetic production jaundice, icterus neonatorum probably a combination of production and retention jaundice. Obstruction jaundice is a combination of lymphogenic and retention jaundice, whereby the lymphogenic component is initially non-regurgitative, later predominantly regurgitative. Parenchymatous jaundice is likewise a combination of retention and lymphogenic jaundice since the necrosis of the liver cells opens a passage between the bile capillaries and the lymph ducts. The lymphogenic component predominates in all cases of rapidly developing jaundice (obstruction jaundice, parenchymatous jaundice in virus hepatitis), while a severe jaundice can only be regarded as a true retention or production jaundice if it develops gradually in the space of at least a week or more. Experimental observations have shown that a reduction of the bilirubin excretion to 1/3, or a threefold increase in its production, results in jaundice.

In blood, bilirubin is linked to the albumins. It is formed in all the tissues, but principally in the reticuloendothelium. In jaundice it migrates after a certain time into the tissues, where it is retained (presumably linked to elastin). Bilirubin is not absorbed in the gastrointestinal tract but passes unchanged into the small intestine. In the large intestine it is hydrogenated to tetrahydromesobilan (formerly known as stercobilinogen) by bacterial enzymes (dehydrogenase or dead coli bacilli) and hydrogen furnished by cysteine or *Clostridium lentoputrescens*. In therapy involving intestinal sterilization with antibiotics bilirubin can therefore appear unchanged in the faeces. The renal clearance of bilirubin is extremely small and amounts to ca. 0.1–0.5 ml per minute. The threshold value of the bilirubin serum concentration for renal excretion shows marked individual variations and is presumably not the same for a developing and a subsiding jaundice; in haemolytic icterus neonatorum it is higher than in other forms of jaundice. The urinary excretion of urobilin follows a quite different course to that of bilirubin. Urobilin occurs in serum in very small

Remarks on bilirubin¹⁻¹⁵ (continued)

concentrations up to 0.5 mg/100 ml. It is readily eliminated in the urine as well as in the bile. Nothing is known as to its origin.

The theory that the indirect-reacting (VAN DEN BERGH reaction) bilirubin has passed the liver cells but the direct-reacting not, can no longer be maintained in the face of existing knowledge unless an explanation for the existence of two kinds of bilirubin can be found. Clinically, the distinction between direct- and indirect-reacting bilirubin remains both of differential-diagnostic and of prognostic importance, even if the theory of passage through the liver must be abandoned. *Assessment must be made on the basis of the total bilirubin level* (= total indirect-reacting bilirubin) the normal upper limit of which should be regarded as 1 mg/100 ml. When the total bilirubin level is at this figure the determination of the direct-reacting bilirubin is doubly valuable: 1. in differential diagnosis, in that levels below 0.2–0.25 mg/100 ml indicate extrahepatic

jaundice, levels above this figure hepatic (parenchymatous or obstruction) jaundice; 2. *prognostically*, in that a persisting supra-normal level of direct-reacting bilirubin indicates persistence of the hepatic activity even if the indirect-reacting bilirubin level has returned to normal, while a return of the direct-reacting bilirubin level to normal, even when a high total bilirubin level is maintained, points strongly to a regression of the hepatic activity. As already mentioned, these conclusions are valid only when the total bilirubin level barely exceeds the normal upper limit; *when the total bilirubin concentration is markedly increased the direct-reacting bilirubin level ceases to have any significance. The determination of a markedly increased indirect-reacting total bilirubin concentration is of interest, however, inasmuch as concentrations of over 30 mg/100 ml indicate very strongly a parenchymatous jaundice and exclude an obstructive jaundice.*

¹⁾ BAUMGÄRTEL, T., *Arch. inn. Med.*, **1**, 40, 1949. ²⁾ BAUMGÄRTEL, T., *Physiologie und Pathologie des Bilirubinstoffwechsels als Grundlagen der Ikterusforschung*, Stuttgart, 1951. ³⁾ DUCCI, H., in SHERLOCK, S., *Liver Disease*, London, 1951, p. 218 (discussion). ⁴⁾ EDLUND, Y., *Acta chir. scand.*, **96**, Suppl. 136, 1948. ⁵⁾ GRAY et al., *Biochem. J.*, **45**, Proc. XVI, 1949. ⁶⁾ IMÉNEZ-DÍAZ et al., *Bull. Inst. med. Res. Univ. Madr.*, **1**, 111, 1948. ⁷⁾ POPPER, H., in SHERLOCK, S., *Liver Disease*, London, 1951, p. 219 (discussion). ⁸⁾ SBOROW and WATSON, *J. Lab. clin. Med.*, **34**, 1743, 1949. ⁹⁾ SBOROW et al., *ibid.*, **37**, 52, 1951. ¹⁰⁾ SCHAFFNER et al., *Amer. J. med. Sci.*, **219**, 307, 1950. ¹¹⁾ WATSON, C. J., in SHERLOCK, S., *Liver Disease*, London, 1951, p. 219 (discussion). ¹²⁾ WITH, T. K., *Acta med. scand.*, **34**, 25, 1947. ¹³⁾ WITH, T. K., *New Engl. J. Med.*, **238**, 416, 1948. ¹⁴⁾ WITH, T. K., *Acta med. scand.*, Suppl. **234**, 331, 1949. ¹⁵⁾ WITH, T. K., in SHERLOCK, S., *Liver Disease*, London, 1951, p. 202.

Carbohydrates and related substances	Whole blood			Plasma or serum			Methods and bibliography	Remarks
	Mean	Normal range (Mean ± 2 σ)	Standard deviation σ	Mean	Normal range (Mean ± 2 σ)	Standard deviation σ		
“Reducing substances”								In human blood the principal reducing substance, apart from glucose, is glutathione (for content in blood, see page 319). By careful precipitation of the cell constituents and the plasma proteins by means of isotonic sodium sulphate solution the glutathione can be removed since it is linked to the corpuscles (after FOLIN, HERBERT and BOURNE).
Glucose (adults)								
Fasting blood (venous)	83	75–92	4	97	61–130	–	After MILLER and VAN SLYKE, <i>J. biol. Chem.</i> , 114 , 583, 1936, and SOMOGYI, M., <i>ibid.</i> , 174 , 189, 597, 1948; PEDERSEN, J., <i>Acta paediat.</i> , Suppl. 77 , 201, 1949.	
Fasting blood (capillaries)	93	87–99	3	–	max. 180	–		
(newborn)	–	–	–	–	20–30	–		
Glycogen	5.5	1.2–16.2	–	0	0	–	Glycogen: WAGNER, R., <i>Arch. Biochem.</i> , 11 , 249, 1946.	The blood sugar content is <i>increased</i> in diabetes, <i>lowered</i> in hyperinsulinism, ADDISON’s disease, glycogenosis. – In old age the blood-sugar content increases slightly.
Polysaccharides (as hexoses) (see remarks)	–	–	–	102	73–131	–	After SEIBERT and ATNO, <i>J. biol. Chem.</i> , 163 , 511, 1946.	This value is for substances other than glucose which in non-deproteinized serum give a colour reaction with carbazole.
(other than glucosamine)								
(adults)	–	–	–	111	93–126	–	After SHETLAR et al., <i>Proc. Soc. exp. Biol.</i> , 69 , 507, 1948; <i>Cancer Res.</i> , 9 , 515, 1949.	This value is for substances other than glucose which give a colour reaction with tryptophan (thus excluding glucosamine).
(aged persons)	–	–	–	129	104–138	–		
(children 3–8 years)	–	–	–	105	94–118	–		
Glucosamine (total)								
(adults)	–	–	–	67	61–78	–	After SHETLAR et al., <i>Proc. Soc. exp. Biol.</i> , 69 , 507, 1948.	
(aged persons)	–	–	–	81	70–89	–		
(children 3–8 years)	–	–	–	63	52–69	–		
Pentoses								
(total)	–	–	–	2.55	1.81–3.29	0.37	After GREEN et al., <i>Clin. Sci.</i> , 8 , 65, 1949; STONER and GREEN, <i>J. Path. Bact.</i> , 61 , 114, 1949; GREEN et al., <i>ibid.</i> , 61 , 101, 1949.	The first value (total pentoses) corresponds to free pentoses, nucleotide- and nucleoside-pentoses, the second (phosphorylated pentoses) to nucleotide-pentoses alone.
(phosphorylated)	–	–	–	2.19	1.59–2.79	0.30		
Hexuronates (as glucuronic acid)	6.7	4.1–9.3	–	–	0.4–1.4	–	Serum: after DEICHMANN and DIERKER, <i>J. biol. Chem.</i> , 163 , 753, 1946. Whole blood: RATTISH and BULLOWA, <i>Arch. Biochem.</i> , 2 , 381, 1943.	This value is for substances giving a colour reaction with naphthoresorcinol.

Normal values in mg/100 ml, unless otherwise stated

(For definition of the normal range, see footnote page 317)

Lipids*

Lipids*	Whole blood			Plasma or serum			Methods and bibliography	Remarks
	Mean	Normal range (Mean \pm 2 σ)	Standard deviation σ	Mean	Normal range (Mean \pm 2 σ)	Standard deviation σ		
"Total ether-soluble substances"	559	397-722	-	530	385-675	-	BOYD, E. M., <i>J. biol. Chem.</i> , 143 , 131, 1942. THANNHAUSER, S. J., <i>New Engl. J. Med.</i> , 237 , 515, 546, 1947.	At birth the total lipid content of the blood is lower. It rises sharply in the first 3-4 days after birth, reaching the normal adult level after ca. 20 days. The fat content of the blood is very variable and can reach 2000 mg/100 ml after a meal rich in fats.
Fats Neutral fats**	134	85-237	-	-	0-450	-		
Fatty acids, total	-	290-420	-	-	200-450	-		
volatile	1.8	-	-	-	-	-	Serum values after THANNHAUSER, <i>loc. cit.</i> MCCLENDON, J. F., <i>J. biol. Chem.</i> , 154 , 357, 1944; PHILIPSON, A. T., <i>J. Soc. exp. Biol.</i> , 23 , 346, 1947; REID, R. L., <i>Nature</i> , 165 , 448, 1950.	Of the saturated fatty acids palmitic acid has the highest percentage, of the unsaturated fatty acids oleic acid. The content of linoleic, linolenic and arachidonic acids ("vitamin F") amounts to ca. 8% of the total fatty acids.
Steroids								
Total steroids	-	-	-	170	120-230	-	Remarks on the steroids The principal component of the steroid group is cholesterol, then the steroid hormones, bile acids and other, partly unknown, compounds. The steroid fractions listed in the adjacent table (after MONASTERIO and BERTI, <i>Klin. Wschr.</i> , 30 , 111, 1952) are the result of a clear definition on the basis of chemical reactivity. Total steroids = those precipitated by digitonin + those not precipitated by digitonin; the LIEBERMANN-BURCHARD reactive steroids correspond to those usually designated as "total cholesterol"; the LIEBERMANN-BURCHARD reactive steroids precipitated by digitonin correspond to those usually designated "free cholesterol"; the LIEBERMANN-BURCHARD reactive steroids not precipitated by digitonin correspond roughly to the esterified cholesterol; the steroids precipitated by digitonin which are not LIEBERMANN-BURCHARD reactive definitely contain no cholesterol. <i>Micro-method for determining total, free and esterified cholesterol</i> , SCHÖNHEIMER and SPERRY, <i>J. biol. Chem.</i> , 106 , 745, 1934. <i>Simple method for total cholesterol</i> , ABELL et al., <i>J. biol. Chem.</i> , 195 , 357, 1952. Values for total cholesterol in whole blood, BRUN, G. C., <i>Acta med. scand.</i> , 3 , 9, 1939; for total cholesterol in serum, TUCKER and KEYS, <i>J. clin. Invest.</i> , 30 , 869, 1951; all other values from THANNHAUSER, S. J., <i>New Engl. J. Med.</i> , 237 , 515, 546, 1947.	
Precipitated by digitonin	-	-	-	131	100-180	-		
Precipitated by digitonin and LIEBERMANN-BURCHARD reactive	-	-	-	112	80-160	-		
Precipitated by digitonin and not LIEBERMANN-BURCHARD reactive	-	-	-	20	0- 40	-		
Not precipitated by digitonin but LIEBERMANN-BURCHARD reactive	-	-	-	40	0- 80	-		
Total LIEBERMANN-BURCHARD reactive steroids ...	-	-	-	130	80-190	-		
Cholesterol								
Total, 18-56 years	-	129-228	-	237.8	128.2-347.4	54.8		
Total, 18-25 years	-	-	-	188.6	116.0-261.2	36.3		
Total, 45-56 years	-	-	-	261.3	169.9-352.7	45.7		
Free cholesterol	-	-	-	-	40-70	-		
Esterified cholesterol	-	-	-	-	70-75	-		
(as % of total cholesterol)								
for total cholesterol in serum, TUCKER and KEYS, <i>J. clin. Invest.</i> , 30 , 869, 1951; all other values from THANNHAUSER, S. J., <i>New Engl. J. Med.</i> , 237 , 515, 546, 1947.								
For the ratio of cholesterol to phospholipids, see under Phospholipids; for the relation between cholesterol, basal metabolism and protein-bound iodine, see under Iodine, page 329.								
Total cholesterol: physiological variations: the cholesterol level is markedly lower in younger individuals than in older; in pregnancy the cholesterol content of the serum is increased in proportion to the increased total lipid content. Pathological increases: in xanthomatosis, obstruction jaundice, diabetes, lipaemia. A subnormal content has no clinical significance. - 75% of the blood cholesterol is combined with the lipoproteins (cf. Plasma proteins, page 316).								
Cholesteryl esters: lowered in diseases of the liver parenchyma, of prognostic importance in surgery.								
Bile acids	-	2.5-6.0	-	-	0.2-3.0	-	Whole blood: ROWNTREE, GREENE and ALDRICH, <i>J. clin. Invest.</i> , 4 , 545, 1927. Serum: SHERLOCK and WALSH, <i>Clin. Sci.</i> , 6 , 223, 1948.	Increased in obstruction jaundice, then falling with advancing damage to the liver cells. In hepatocellular jaundice lowered as a result of injury to the liver cells which produce the bile acids.
(Whole blood: as glycocholic acid; serum: as cholic acid)								
Bile salts	-	-	-	-	5-12	-	SHATTUCK, KATAYAMA and KILLIAN, <i>Amer. J. med. Sci.</i> , 175 , 103, 1928.	According to this method the renal threshold value for bile salts is 20 mg/100 ml serum, which explains partly the absence of these salts in the urine of many patients with chronic liver disease.
(as sodium glycocholate)								
Phospholipids								
(phosphatides)								
(see also under Phosphorus, page 326)								
Total	-	-	-	200	150-250	-	THANNHAUSER, S. J., <i>New Engl. J. Med.</i> , 237 , 515, 1947; TAUROG et al., <i>J. biol. Chem.</i> , 156 , 385, 1944.	Phospholipids = lecithin + cephalin + sphingomyelin. The ratio of phospholipid-P to free cholesterol according to ALBRICH et al., <i>J. clin. Invest.</i> , 29 , 781, 1950 is: (phospholipid-P minus 3.7)/free cholesterol = 0.106 (for values expressed in mg/100 ml); in pregnancy this ratio has the range 0.067-0.182 with mean 0.113.
Lecithin	-	-	-	-	100-200	-		
Cephalin	65	31-118	-	-	0- 30	-	THANNHAUSER, <i>loc. cit.</i> ; THANNHAUSER et al., <i>J. biol. Chem.</i> , 129 , 709, 1939; TAUROG, <i>loc. cit.</i> ; HACK, M. H., <i>ibid.</i> , 169 , 137, 1947; SINCLAIR, R. G., <i>ibid.</i> , 174 , 343, 1948; KIRK, J. E., <i>ibid.</i> , 123 , 637, 1938.	
Sphingomyelin	-	-	-	-	10- 30	-		

* Lipids = total matter soluble in ether-alcohol, i.e. neutral fats, fatty acids, steroids, phospholipids, etc.

** Neutral fats = glyceryl esters of higher fatty acids.

Products of intermediary metabolism	Whole blood			Plasma or serum			Methods and bibliography	Remarks
	Mean	Normal range (Mean ± 2 σ)	Standard deviation σ	Mean	Normal range (Mean ± 2 σ)	Standard deviation σ		
Acetone bodies (non-fasting blood)	–	–	–	–	–	–	The content of acetone bodies in the blood corpuscles is very low and the concentration in whole blood is ca. 20% less than that in plasma. – Greatly increased in ketosis, also in diabetes and hunger. The acetone bodies consist for the main part of β-hydroxybutyric acid and acetoacetic acid; acetone is present only in traces.
Total, as β-hydroxybutyric acid	0.5	–	–	–	0.3–0.9	–	WEICHSSELBAUM and SOMOGYI, <i>J. biol. Chem.</i> , 140 , 5, 1941.	
Acetoacetic acid	–	–	–	–	0.8–2.8	–	ROSENTHAL, S. M., <i>ibid.</i> , 179 , 1235, 1949.	
Total α-keto-acids								
(Adults)	1.3	0 –3.1	–	–	0.6–2.1	–	Serum: WESTERKAMP, H., <i>Biochem. Z.</i> , 263 , 239, 1933; whole blood, adults: FRIEDEMANN and HAUGEN, <i>J. biol. Chem.</i> , 147 , 415, 1943; whole blood, newborn: ALLIBONE and FINCH, <i>Arch. Dis. Childb.</i> , 21 , 165, 1946.	
(Newborn)	0.8	0.6–1.0	–	–	–	–		
α-Ketoglutaric acid ..	0.2	–	–	0.8	–	–	Whole blood: CAVALLINI et al., <i>Nature</i> , 164 , 792, 1949; serum: KREBS, H. A., <i>Biochem. J.</i> , 32 , 108, 1938.	See Pyruvic acid, below.
Pyruvic acid	0.76	0.414–1.106	0.173	1.1	0.5–1.7	0.3	Whole blood: KLEIN, J. R., <i>J. biol. Chem.</i> , 145 , 35, 1942; Serum: KIRK and CHIEFFI, <i>J. Nutr.</i> , 38 , 353, 1949 (249 tests).	The pyruvic acid level in blood does not change with age. It is increased (together with all α-keto-acids and lactic acid) in vitamin-B ₁ deficiency (cf. page 215), after muscular activity, great emotional excitement, in alkalosis, dyspnoea, cardiovascular disturbances, thyrotoxicosis.
<p>According to HORWITT and KREISLER, <i>J. Nutr.</i>, 37, 411, 1949, examination for vitamin-B₁ deficiency is therefore best made as follows: after intake of 1.8 g glucose per kg body weight and gentle stair-climbing for 60 minutes, the glucose (G), lactic acid (L) and pyruvic acid (P) contents of the blood are determined as mg/100 ml. The glucose–lactic acid–pyruvic acid index (carbohydrate metabolism index or CMI) is then given by the formula:</p> $\text{CMI} = \frac{1}{2} \left(L - \frac{G}{10} + 15 P - \frac{G}{10} \right)$ <p>A CMI of 15 is the upper limit of the normal range. Higher values are a certain indication of vitamin-B₁ deficiency.</p>								
Lactic acid	9.9	4.7–15.1	2.6	11.5	6.1–16.9	2.7	GIBBS et al., <i>J. biol. Chem.</i> , 144 , 325, 1942.	Sec Pyruvic acid, above.
Citric acid								
(Adults)	1.9	1.3–2.5	–	2.4	1.6–3.2	–	NATELSON et al., <i>J. clin. Invest.</i> , 27 , 446, 1948.	
(Children)	–	–	–	2.8	1.8–3.8	–		
(Newborn)	–	–	–	–	3 –6	–		
Malic acid	0.46	0.24–0.75	–	0.5	0.1–0.9	–	HUMMEL, J. P., <i>J. biol. Chem.</i> , 180 , 1225, 1949.	
Succinic acid	–	–	–	0.5	–	–	KREBS, H. A., <i>Ann. Rev. Biochem.</i> , 9 , 417, 1950.	
Fumaric acid	<0.3	–	–	–	–	–	MARSHALL et al., <i>J. biol. Chem.</i> , 179 , 1127, 1949.	

Normal values in mg/100 ml, unless otherwise stated

(For definition of the normal range, see footnote page 317)

	Whole blood			Plasma or serum			Methods, bibliography, remarks
	Mean	Normal range (Mean \pm 2 σ)	Standard deviation σ	Mean	Normal range (Mean \pm 2 σ)	Standard deviation σ	
Alcohol (ethyl alcohol)	+	always abnormal	-	-	-	-	<i>Effect of alcohol:</i> intoxicating effect very variable from person to person; HARGER, R. N., <i>J. Criminal Law and Criminology</i> , 35 , 202, 1944, gives the following figures (in g/100 ml blood): 0–0.05 (ca. 2 oz. whisky) safe; 0.05–0.15 (ca. 6 oz. whisky) questionable; 0.15–0.5 drunk; over 0.5 dead drunk; over 0.55 fatal.
Hormones							
Adrenaline, noradrenaline ...	-	-	-	-	-	-	Cf. pages 205 and 206.
Androgens	-	-	-	-	-	-	Cf. page 201.
Pituitary hormones	-	-	-	-	-	-	Cf. pages 179–194.
Insulin	-	-	-	-	-	-	Cf. page 207.
Adrenocortical hormones ...	-	-	-	-	-	-	Cf. pages 182–191, 203.
Oestrogens	-	-	-	-	-	-	Cf. pages 201 and 202.
Thyroxine	-	-	-	-	-	-	Cf. pages 207 and 208.
Vitamins							
Fat-soluble vitamins							
Vitamin A	-	-	-	0.025	0.01–0.036	-	HUME and KREBS, <i>Spec. Rep. Ser. Med. Res. Conn. (Lond.)</i> , No. 264, 1, 1949; KIRK and CHIEFFI, <i>J. Nutr.</i> , 36 , 315, 1948.
(as carotenes)	0.120	0.02–0.30	-	-	-	-	
Carotenes, total	-	-	-	0.09	0.06–0.18	-	HUME and KREBS, <i>loc. cit.</i> , KIRK and CHIEFFI, <i>loc. cit.</i> Carotenes and vitamin A, cf. page 209.
Vitamin D (as D ₂)	-	-	-	0.0028	0.0017–0.0041	-	WARKANY and MABON, <i>Amer. J. Dis. Child.</i> , 60 , 606, 1940. Cf. page 210.
Vitamin E	-	-	-	1.1	0.5–1.59	-	DARBY et al., <i>Ann. N. Y. Acad. Sci.</i> , 52 , 328, 1949; QUAIFFE et al., <i>J. biol. Chem.</i> , 180 , 1229, 1949. – Cf. page 211.
Water-soluble vitamins							
Vitamin B ₁ (thiamine)	0.0075	0.0035–0.0115	0.002	-	0–0.0013	-	<i>Whole blood:</i> EVERETT, M. R., <i>Medical Biochemistry</i> , New York, 1946; <i>serum:</i> MEIKLEJOHN, A. P., <i>Biochem. J.</i> , 31 , 1441, 1938. – Occurs mainly in the corpuscles as cocarboxylase; on the latter (general) see page 214, (blood) see the next page.
Vitamin B ₂ (riboflavin) ...	0.027	0.013–0.085	-	0.0008	0.0003–0.013	-	Values include mononucleotide of riboflavin, expressed as free vitamin. <i>Whole blood:</i> <i>Oxford Nutritional Survey</i> , 1947; <i>serum:</i> BURCH et al., <i>J. biol. Chem.</i> , 175 , 457, 1948. – Cf. page 215.
Vitamin B ₆ (pyridoxine) ..	0.011	0.005–0.020	-	0.008	0.001–0.018	-	GREENBERG and RINEHART, <i>Proc. Soc. exp. Biol.</i> , 70 , 20, 1949. Cf. page 217.
Vitamin B ₁₂	0.00008	0.00006– 0.00014	-	-	-	-	COUCH et al., <i>Amer. J. Physiol.</i> , 163 , 77, 1950. – Cf. page 221.
Biotin	0.00123	0.0008–0.0017	-	0.000127	0.00095– 0.00166	-	DENKO et al., <i>Arch. Biochem.</i> , 13 , 481, 1947. – Cf. page 218.
Choline (total)	-	-	-	-	26–35	-	LUECKE and PEARSON, <i>J. biol. Chem.</i> , 153 , 259, 1944 (also for free choline in whole blood).
(free)	2.5	1.0–4.0	-	-	0.2–2	-	APPLETON et al., <i>Fed. Proc.</i> , 10 , 157, 1951. Lower values in summer, maximum in February/March. Choline and acetylcholine, see page 222 and (blood) page 318.
Folic acid (pteroylglutamic acid) (total)	0.0035	0.0023–0.053	-	0.00175	0.0017–0.0050	-	DENKO et al., <i>Arch. Biochem.</i> , 13 , 481, 1947; SCHWEIGERT and PEARSON, <i>Amer. J. Physiol.</i> , 148 , 319, 1947; SIMPSON and SCHWEIGERT, <i>Arch. Biochem.</i> , 20 , 32, 1949. – Cf. pages 219 and 220.
(free)	0.000085	0.00005– 0.00013	-	0.00005	-	-	
mesoInositol	-	-	-	0.50	0.37–0.76	-	SONNE and SOBOTKA, <i>Arch. Biochem.</i> , 14 , 93, 1947. – Cf. page 223.
Nicotinic acid (niacin)	0.6	0.2–0.9	-	0.075	0.025–0.15	-	Includes nicotinic acid, nicotinamide, codehydrogenase I and II but excludes N ¹ -methylnicotinamide and trigonelline. Values from KOCHHAR, B. D., <i>Indian J. med. Res.</i> , 28 , 385, 1940; ROGGEN, J. C., <i>Ned. T. Geneesk.</i> , 85 , 4603, 1941; OLIVA and MAGRINI, <i>Boll. Soc. ital. Biol. sper.</i> , 16 , 245, 1941; KOCHHAR, B. D., <i>Ann. Biochem. exp. Med.</i> , 2 , 211, 1942; RAOUL et al., <i>C. R. Soc. Biol.</i> , 136 , 740, 1942; CARTER and O'BRIEN, <i>Quart. J. Med.</i> , 14 , 197, 1945. – Cf. pages 217 and 218. Diphosphopyridine nucleotide in blood, see the next page.
Pantothenic acid	0.020	0.018–0.034	-	0.012	0.006–0.022	-	<i>Whole blood:</i> STANBERG et al., <i>J. biol. Chem.</i> , 135 , 353, 1940; <i>serum:</i> DENKO et al., <i>Arch. Biochem.</i> , 13 , 481, 1947. – Cf. page 216. Coenzyme A, see the next page.

Normal values in mg/100 ml, unless otherwise stated

(For definition of the normal range, see footnote page 317)

Vitamins (continued)	Whole blood			Plasma or serum			Methods, bibliography, remarks
	Mean	Normal range (Mean ± 2σ)	Standard deviation σ	Mean	Normal range (Mean ± 2σ)	Standard deviation σ	
Vitamin C	0.62	0.2–0.7	–	–	0.1–0.7	–	<i>Whole blood:</i> OSBORNE et al., <i>J. Lab. clin. Med.</i> , 27 , 1135, 1942; <i>serum:</i> Vitamin C Sub-Committee, Medical Research Council, <i>Lancet</i> , 1 , 853, 1948. – Cf. page 213. Plasma values in relation to vitamin-C intake: Daily intake Plasma value 0 mg < 0.03 mg/100 ml 5 ” < 0.05 ” ” ” 10 ” < 0.10 ” ” ” 20 ” 0.10 ” ” ” 50 ” 0.31 ” ” ” 70 ” 0.55 ” ” ” 600 ” 1.02 ” ” ” KAPLAN and LIPMANN, <i>J. biol. Chem.</i> , 174 , 37, 1948.
Coenzymes							
Coenzyme A (as combined pantothenic acid)	–	(erythrocytes:) 0.210–0.280	–	–	–	–	
Cocarboxylase							
(1)	0.007	0.0028–0.0112	–	–	–	–	(1) <i>Method:</i> manometric determination of CO ₂ from pyruvate; values from GOODHART and SINCLAIR, <i>Biochem. J.</i> , 33 , 1099, 1939; (2) <i>microbiological method</i> , values from BEERSTECHEER and SPANGLER, in ALBRITTON, E. C., <i>Standard Values in Blood</i> , Philadelphia, 1952. (3) Values from SMITS and FLORIJN, <i>Biochim. biophys. Acta</i> , 3 , 44, 1949.–The corpuscles of men contain considerably more than those of women.– Cf. page 214.
(2) Men	0.0089	–	–	–	–	–	
(2) Women	0.0076	–	–	–	–	–	
(2) Men	0.010	(erythrocytes:) 0.007–0.014	–	–	–	–	
(2) Women	0.0065	0.005–0.008	–	–	–	–	
(3) (as free thiamine)	–	(in 10 ¹¹ erythrocytes:) 0.0021–0.0045	–	–	–	–	
(3) (as free thiamine)	–	(in 10 ¹¹ leucocytes:) 0.34–0.28	–	–	–	–	
Flavine adenine dinucleotide (riboflavin dinucleotide)	0.075	(erythrocytes:) –	–	0.010	–	–	KLEIN and KOHN, <i>J. biol. Chem.</i> , 136 , 177, 1940. – Cf. pages 215 and 216.
Pyridine nucleotides, total (nucleotides of nicotinic acid) as diphosphonucleotide (DPN)	3.6 7.7	(whole blood:) 2.6–4.6 (erythrocytes:) 6.1–9.3	– –	0.070	0.020–0.120	–	LEVITAS et al., <i>J. biol. Chem.</i> , 167 , 169, 1947. – The ratio of di-phosphonucleotide (DPN) to triphosphonucleotide (TPN) is estimated to be 8:1.

Enzymes

Normal values in enzyme units per 100 ml

							Methods and bibliography	Remarks
Adenosinepoly- phosphatase								
acid } see remarks	–	–	–	41	21–61	–	MEISTER, A., <i>Science</i> , 106 , 167, 1947; <i>J. clin. Invest.</i> , 26 , 263, 1948.	Expressed in μmol phosphorus per hour, at pH 4.8 (acid) and pH 8.9 (alkaline).
alkaline }	–	–	–	30	10–51	–		
Aldolase	–	–	–	490	350–800	–	SIBLEY and LEHNINGER, <i>J. biol. Chem.</i> , 177 , 859, 1949.	Expressed in μg fructose diphosphate per hour, at pH 8.6 and 38°C.
Amylase (diastase) . . . (as mg glucose/100 ml serum or plasma, i.e. the glucose content of the serum is determined, the serum mixed with starch, in- cubated for 15 or 30 min and the glucose content again de- termined. The difference, i.e. 2nd value less 1st value, is the amylase content expressed as the amount of glucose formed from the starch).	– –	– –	– –	– –	40–145 (15 min incubation) 95–250 (30 min incubation)	– –	LEWISON, E. F., <i>Surg. Gynec. Obstet.</i> , 72 , 202, 1941; ANDERSCH, M. A., <i>J. biol. Chem.</i> , 166 , 705, 1946.	Increased in pancreatic disease (if the renal function is intact, i.e. when the urinary excretion of amylase is likewise increased) and in severe renal insufficiency (pancreatic function normal, renal excretion low). – Of differential-diagnostic importance is the fact that opiates (e.g. codeine sulphate) can markedly increase the serum amylase (and lipase) content for 24 hours after administration (GROSS et al., <i>Proc. Mayo Clin.</i> , 26 , 81, 1951).
Arginase	2000	800–3200	–	–	–	–	KOCHAKIAN et al., <i>Conf. Metabolic Aspects Con-valescence</i> , 17 , 187, 1948; KOCHAKIAN, C. D., <i>J. biol. Chem.</i> , 155 , 579, 1944.	Expressed in KOCHAKIAN's units. – The arginase content is lowered in undernourishment.

Normal values in enzyme units per 100 ml

(For definition of the normal range, see footnote page 317)

	Whole blood			Plasma or serum			Methods and bibliography	Remarks
	Mean	Normal range (Mean \pm 2 σ)	Standard deviation σ	Mean	Normal range (Mean \pm 2 σ)	Standard deviation σ		
Catalase	-	-	-	690	420-950	-	DILLE and WATKINS, <i>J. Lab. clin. Med.</i> , 33 , 480, 1948.	Expressed in DILLE's units.
Cholinesterase								
(expressed in Δ pH per hour = fall in pH units per hour)		(erythrocytes:)					Electrometric methods of GLICK, D., <i>Biochem. J.</i> , 31 , 521, 1937; SANZ, M., <i>Helv. physiol. pharmacol. Acta</i> , 2 , C 29, 1944; RADOUCO, C., and FROMMEL, E., <i>ibid.</i> , 10 , 339, 1952.	Values from SCUDAMORE, H. H., <i>J. Lab. clin. Med.</i> , 37 , 860, 1951 (cf. Acetylcholine, page 318).
Healthy subjects	0.67	0.47-0.87	0.10	0.94	0.56-1.31	0.19		
Asthmatics	0.68	0.22-1.12	0.22	0.96	0.76-1.16	0.10		
Dehydropeptidase ...	-	-	-	359	191-527	-	MEISTER and GREENSTEIN, <i>J. nat. Cancer Inst.</i> , 8 , 169, 1948.	Expressed in μ mol NH ₃ per $\frac{1}{2}$ hour, substrate DL-alanyldehydroalanine at pH 8.1 and 37°C.
β -Glucuronidase								
Men	-	-	-	-	0-181	-	FISHMAN et al., <i>J. biol. Chem.</i> , 173 , 449, 1948.	Expressed in μ g phenolphthalein per hour, substrate phenolphthalein-glucuronide at pH 4.5 and 37°C.
Women	-	-	-	-	37-230	-		
Glyoxalase	611.7 1398	425-705 (erythrocytes:) 1320-1500	- -	- -	- -	- -	COHEN and SOBER, <i>Cancer Res.</i> , 5 , 631, 1945.	Expressed in ml CO ₂ per 20 min, substrate methylglyoxal at pH 7.2 and 26°C, in presence of glutathione.
Histaminase	36	30-40	-	18	0-36	-	WERLE and EFFKE-MANN, <i>Klin. Wschr.</i> , 19 , 717, 1940.	Expressed in μ g histamine destroyed in 90 min at 37°C. - Increased in pregnancy.
Lipase	-	-	-	-	0-150	-	COMFORT and OSTERBERG, <i>Med. Clin. N. Amer.</i> , 24 , 1137, 1940.	Expressed in ml 0.05-N NaOH per 24 hours, substrate olive oil emulsion. - The serum lipase level varies similarly to the amylase level. Cf. the opposite page.
Phenolsulphatase	-	-	-	-	30-1550	-	HUGGINS and SMITH, <i>J. biol. Chem.</i> , 170 , 391, 1947.	
Phosphatase								
alkaline	-	-	-	-	2.2-8.6	-	SHINOWARA et al., <i>J. biol. Chem.</i> , 142 , 921, 1942.	The unit of SHINOWARA et al. is defined as the amount of enzyme which on incubation for one hour on a substrate containing sodium β -glycerophosphate at 37°C liberates phosphate ion equivalent to 1 mg phosphorus; for acid phosphatase the optimum pH of the reaction medium is 5.00 \pm 0.15; for alkaline phosphatase 9.30 \pm 0.15. According to BESSEY, O., in GRÖRCY, P., <i>Vitamin Methods</i> , New York, 1951, p. 316, the optimum pH for alkaline phosphatase is 10.0-10.1.
acid	-	-	-	-	0-1	-		
								Alkaline phosphatase occurs in highest concentration in the prostate, bone marrow, kidneys, liver and intestinal mucosa, as also in the erythrocytes.
								The alkaline phosphatase in serum is increased in active bone-marrow disease, in rickets, in obstruction jaundice.
								The acid phosphatase is usually increased in cases of prostate carcinoma metastases; treatment with oestrogens brings about a reduction in several weeks.
Profibrinolysin	-	-	-	-	50-125	-	GUEST et al., <i>Amer. J. Physiol.</i> , 150 , 661, 1947.	Expressed in fibrinolysin units.
Pteroylglutamic acid conjugase	-	-	-	-	80-100	-	WOLFF et al., <i>Science</i> , 109 , 612, 1949.	Expressed in μ g folic acid produced in 90 min from yeast extract at pH 4.5 and 37°C.
(Folic acid conjugase)								

Normal values in mg/100 ml, unless otherwise stated
(For definition of the normal range, see footnote page 317)

Inorganic constituents – Acid-formers

(other than trace elements)

Phosphorus, P

(1) Total (as P)

Inorganic (as P)

(2) Adults

(1) Children (age 3–13) .

Organic or ester phosphorus (as P)

Lipid phosphorus (as P) . .

Adenosine triphosphate (ATP) phosphorus (as P)

Diphosphoglycerate phosphorus (as P)

Nucleotide phosphorus (as P)

Hexose phosphate phosphorus (as P)

Sulphur, S

(other than protein-S)

Total (as S)

Inorganic (as S)

Conjugated sulphur (as S) .

Neutral sulphur (as S)

Chlorides (as Cl)

Chlorides in mg. equiv/l .
in mg/100 ml .

	Whole blood			Plasma or serum		
	Mean	Normal range (Mean ± 2σ)	Standard deviation σ	Mean	Normal range (Mean ± 2σ)	Standard deviation σ
(1) Total (as P)	-	28–48	-	12.1	10.0–14.1	-
Inorganic (as P)						
(2) Adults	2.9	2.1–3.8	-	3.2	2.4–4.4	-
	2.4	(erythrocytes:) 0.91–3.3	-	-	-	-
(1) Children (age 3–13) .	-	-	-	5.7	4–7	-
Organic or ester phosphorus (as P)	23.1	18.6–29	-	0.6	0–4	-
	50	(erythrocytes:) 39–59	-	-	-	-
Lipid phosphorus (as P) . .	11.2	8–18	-	8.0	6.1–9.9	-
Adenosine triphosphate (ATP) phosphorus (as P)	8.1	5.1–10.4	-	-	-	-
Diphosphoglycerate phosphorus (as P)	12.4	8.1–16.7	-	-	-	-
Nucleotide phosphorus (as P)	2.8	2.2–3.4	-	-	-	-
Hexose phosphate phosphorus (as P)	3.2	1.4–5.0	-	-	-	-
Total (as S)	-	3.84–5.06	-	3.38	2.95–3.75	-
Inorganic (as S)	-	0.28–0.65	-	1.57	1.00–1.85	-
Conjugated sulphur (as S) .	-	0.07–0.96	-	0.39	0.25–0.65	-
Neutral sulphur (as S)	-	3.19–4.32	-	1.42	0.90–1.95	-
Chlorides in mg. equiv/l .	-	76.1–90.2	-	102.9	100.1–107.4	-
in mg/100 ml .	-	270–320	-	365	355–381	-

Methods and bibliography	Remarks
(1) STEARNS and WARWEG, <i>J. biol. Chem.</i> , 102 , 749, 1933. (2) HELVE, O., <i>Acta med. scand.</i> , 125 , 505, 1946.	The plasma phosphorus level in adolescence (controlled by the concentration of inorganic phosphorus) is markedly higher than in adults, owing to the requirements of bone calcification (cf. Growth hormone, page 192). <i>Lowered</i> in rickets; often in osteomalacia; in osteitis fibrosa; in hyperparathyroidism; through insulin. <i>Increased</i> in chronic nephritis; in diabetic coma; after severe bone fractures.
Whole blood: HELVE, O., <i>Acta med. scand.</i> , 125 , 505, 1946. Serum: STEARNS and WARWEG, <i>J. biol. Chem.</i> , 102 , 749, 1933.	= acid-soluble phosphates, except inorganic orthophosphates.
STEARNS and WARWEG, <i>J. biol. Chem.</i> , 102 , 749, 1933.	= organic phosphates soluble in ether-alcohol or ether. Lipid-P × 25 = lecithin Lipid-P × 23.5 = phospholipids
KERR and DAOUD, <i>J. biol. Chem.</i> , 109 , 301, 1935.	For adenosine triphosphate in blood, see page 318.
HELVE, O., <i>Acta med. scand.</i> , 125 , 505, 1946.	
KERR and DAOUD, <i>J. biol. Chem.</i> , 109 , 301, 1935.	
HELVE, O., <i>Acta med. scand.</i> , 125 , 505, 1946.	
STURM and POTHMANN, <i>Z. klin. Med.</i> , 137 , 467, 1940.	
STURM, <i>loc. cit.</i> ; POWER and WAKEFIELD, <i>J. biol. Chem.</i> , 123 , 665, 1938.	Increased in renal insufficiency. Cf. Inorganic sulphates in urine, page 290).
STURM, <i>loc. cit.</i>	= organic substances from which sulphates are liberated by acid hydrolysis (= sulphuric esters of carbohydrates and phenols).
STURM, <i>loc. cit.</i>	= substances which are converted into sulphates by oxidation (S-containing amino-acids, taurine, thiosulphate, thiocyanate, thiamine).
HALD et al., <i>J. clin. Invest.</i> , 26 , 983, 1947; SNYDER and KATZENELBOGEN, <i>J. biol. Chem.</i> , 143 , 223, 1942. – For a new method, see HÜBENER and SCHMIDT, <i>Hoppe-Seyl. Z. physiol. Chem.</i> , 289 , 67, 1952.	<i>Reduced</i> after severe vomiting, severe burns, in ADDISON's disease, mercury poisoning, pneumonia. <i>Increases</i> are of no diagnostic significance. – After operations: an immediate drop in the whole-blood chloride level, accompanied by a variable reduction in the plasma level, is followed by a rise in the whole-blood level above the normal value. Similar changes occur in the sodium content of whole blood (WILKINSON et al., <i>Lancet</i> , 1 , 315, 1951). The increase in chlorides is due to stimulation of the pituitary-adrenal system.
As soon as whole blood comes into contact with air CO ₂ migrates from the erythrocytes and is replaced by Cl-ions from the plasma ("chloride shift"). The true chloride content of plasma can therefore only be determined when the whole process up to the separation of the erythrocytes is carried out in the absence of air.	

Normal values in mg/100 ml, unless otherwise stated

(For definition of the normal range, see footnote page 317)

Inorganic constituents – Base-formers
(other than trace elements)**Total bases**

(in mg. equiv/litre) (1)

(in mg. equiv/litre) (2)

Sodium, Na

(in mg. equiv/litre)

(in mg/100 ml)

Magnesium, Mg

(in mg. equiv/litre)

(in mg/100 ml)

Silicon, Si (as SiO₂)

Men (240 tests)

Women (54 tests)

Men and women as one group

(264 tests)

Potassium, K

(in mg. equiv/litre)

(in mg/100 ml)

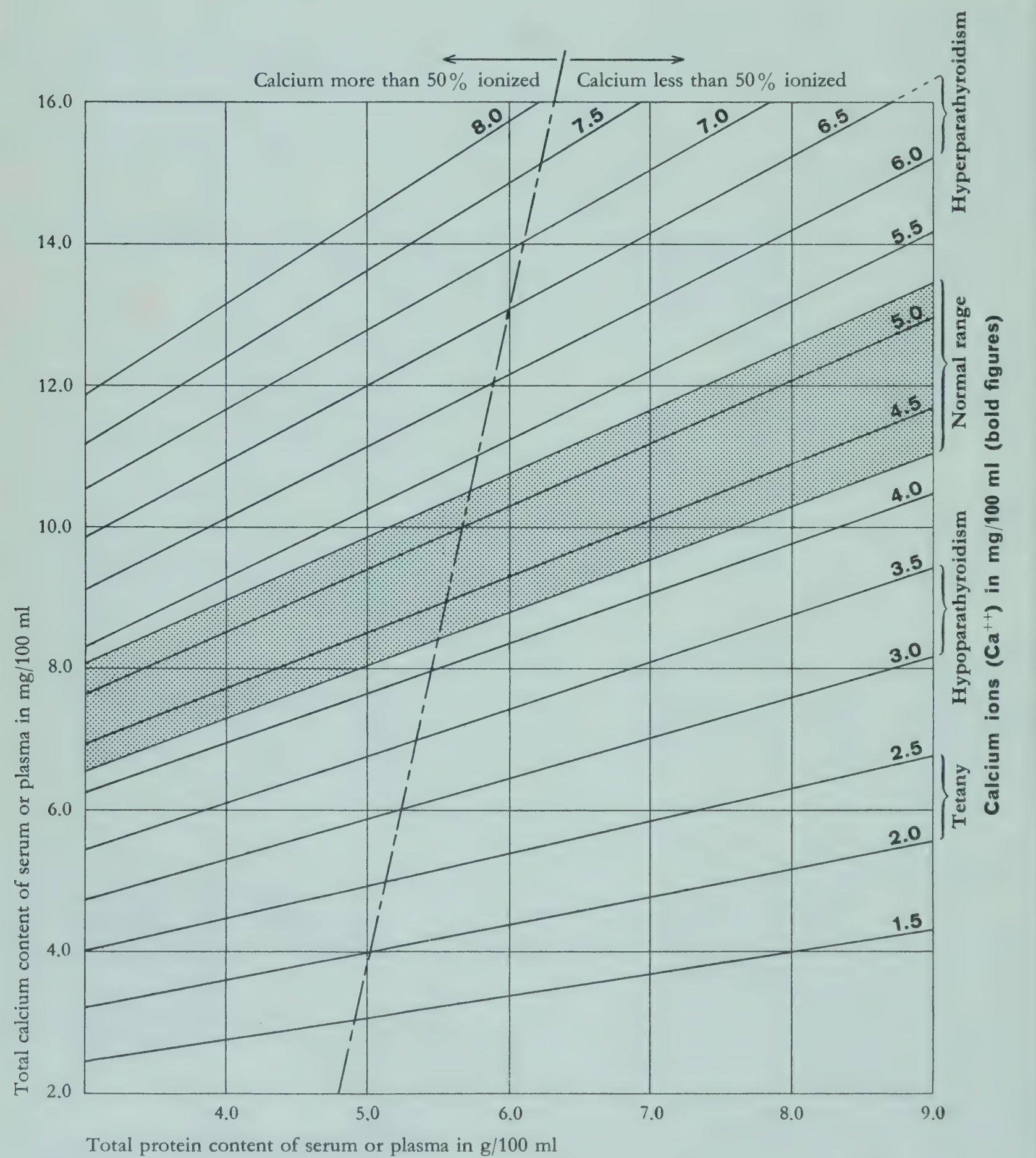
Calcium, Ca

Total

Ionized Ca

	Whole blood			Plasma or serum			Methods and bibliography	Remarks
	Mean	Normal range (Mean \pm 2 σ)	Standard deviation σ	Mean	Normal range (Mean \pm 2 σ)	Standard deviation σ		
(in mg. equiv/litre) (1)	–	–	–	152.0	147.6–156.0	–	(1) After TALBOTT, quoted by SUNDERMAN and BOERNER, <i>Normal Values in Clinical Medicine</i> , Philadelphia, 1950.	(1) Sum of all the cations. Higher in premature infants (mean 159 mg. equiv/l) according to REARDEN et al., <i>Amer. J. Dis. Child.</i> , 79 , 372, 1950.
(in mg. equiv/litre) (2)	–	–	–	146.5	144.0–149.0	–	(2) After SUNDERMAN and BOERNER, <i>loc. cit.</i>	(2) Calculated from the electrical conductivity (see page 308).
(in mg. equiv/litre)	85	79.3–91.0 (erythrocytes:)	–	144.7	135–155	5	Method of MOSHER et al., <i>Amer. J. clin. Path.</i> , 19 , 461, 1949. Values from (whole blood) HALD, J., <i>J. biol. Chem.</i> , 167 , 499, 1947; (serum) ELLIOTT and HOLLEY, <i>Fed. Proc.</i> , 10 , 180, 1951 (400 tests) in agreement with SMITH et al., <i>Amer. J. clin. Path.</i> , 20 , 263, 1950; MARINIS et al., <i>J. Lab. clin. Med.</i> , 32 , 1208, 1948; OVERMAN et al., <i>J. biol. Chem.</i> , 168 , 641, 1947; HALD, J., <i>ibid.</i> , 167 , 499, 1947.	See remarks under Chlorides and Potassium.
	21.2	15.7–25.3 (whole blood:)	–	–	–	–		
(in mg/100 ml)	195.5	182.4–199.3 (erythrocytes:)	–	333	310.5–356.5	11.5		
	48.8	36.1–58.2	–	–	–	–		
(in mg. equiv/litre)	–	–	–	1.58	1.34–1.82	0.12	SIMONSEN et al., <i>J. biol. Chem.</i> , 169 , 39, 1947, in agreement with SMITH et al., <i>Amer. J. clin. Path.</i> , 20 , 263, 1950.	Increased in starvation up to 40% (SUNDERMAN, F. W., <i>Amer. J. clin. Path.</i> , 17 , 169, 1947).
(in mg/100 ml)	–	–	–	1.93	1.65–2.22	0.146		
Men (240 tests)	8.4	3.6–13.2	2.4	–	–	–	Method of URBACH, <i>Mikrochem.</i> , 14 , 199, 1934, modified by KRAUT and WEBER, <i>Hoppe-Seyl. Z. physiol. Chem.</i> , 275 , 127, 1942. Values from WORTH, G., <i>Klin. Wschr.</i> , 30 , 82, 1952.	No significant age, sex or pathological differences.
Women (54 tests)	8.0	3.0–13.0	2.5	–	–	–		
Men and women as one group (264 tests)	8.3	3.5–13.1	2.4	–	–	–		
(in mg. equiv/litre)	44.8	40.3–48.8 (erythrocytes:)	–	4.18	3.1–5.5	0.6	<i>Whole blood</i> : after HALD, P. M., <i>J. biol. Chem.</i> , 167 , 499, 1947. <i>Serum</i> : after ELLIOTT and HOLLEY, see under Sodium.	Potassium is mainly intracellular, sodium extracellular. <i>Increased</i> (serum) in ADDISON's disease and in uraemia with renal retention. <i>Lowered</i> in diarrhoea, in diseases accompanied by acute tissue breakdown, in kidney injury, in alimentary K-deficiency, inter alia through intravenous feeding without K (MARTIN et al., <i>Calif. Med.</i> , 72 , 133, 1950, 390 cases).
	95.1	91.8–100.0 (whole blood:)	–	–	–	–		
(in mg/100 ml)	175.2	157.6–190.8 (erythrocytes:)	–	16.34	12.12–21.5	2.3		
	371.8	358.9–391	–	–	–	–		
Total	–	5–7	–	10.0	8.2–11.6	–	HALD, P. M., <i>J. biol. Chem.</i> , 103 , 471, 1933; SNYDER and KATZEN-ELBOGEN, <i>ibid.</i> , 143 , 223, 1942.	<i>Lowered</i> in tetany (infantile, rachitic or following parathyroidectomy), vitamin-D deficiency. <i>Increased</i> after excessive doses of parathyroid hormone or vitamin D overdosage of long duration. –The blood corpuscles contain practically no calcium.
Ionized Ca	–	–	–	4.8	4.25–5.25	–	McLEAN and HASTINGS, <i>Amer. J. med. Sci.</i> , 189 , 601, 1935. Titrimetric method, see BUCKLEY et al., <i>J. Lab. clin. Med.</i> , 38 , 751, 1951.	

Nomogram for the calculation of calcium ions (Ca^{++}) from the total protein and total calcium content of the serum or plasma. After McLEAN and HASTINGS, *Amer. J. med. Sci.*, 189, 601, 1935.



Normal values in mg/100 ml, unless otherwise stated
(For definition of the normal range, see footnote page 317)

Inorganic constituents – Trace elements

	Whole blood			Plasma or serum			Methods and bibliography	Remarks
	Mean	Normal range (Mean ± 2σ)	Standard deviation σ	Mean	Normal range (Mean ± 2σ)	Standard deviation σ		
Fluorine, F	0.028	0.011–0.045	–	0.028	0.010–0.045	–	Values from LARGENT and CHOLAK, quoted by LARGENT in ALBRITTON, E. C., <i>Standard Values in Blood</i> , Philadelphia, 1952.	
Bromine, Br	–	0.0007–0.001	–	–	–	–	GRAY and MOORE, <i>J. Lab. clin. Med.</i> , 27 , 680, 1942.	Increased after bromine medication.
Iodine, I								
(Total, adults)	0.0077	0.003–0.013	–	0.0071	0.0048–0.0086	–	KLEIN, E., <i>Ärztl. Wschr.</i> , 5 , 967, 1950. TAUROG and CHAIKOFF, <i>J. biol. Chem.</i> , 163 , 313, 1946. TALBOT et al., <i>ibid.</i> , 153 , 479, 1944. ORR and LEITCH, <i>Spec. Rep. Ser. Med. Res. Coun. (Lond.)</i> , 123 , 1939.	In human <i>plasma</i> the levels of total and protein-bound iodine are practically identical, in contrast to other species such as chickens and dogs. – The protein-bound iodine consists of two fractions resembling respectively thyroxine and di-iodotyrosine. It is an excellent measure of thyroid activity, particularly in cases where this cannot be judged from the basal metabolism, as for example in ACTH therapy. Values under 0.004 are indicative of hypothyreosis.
(Total, children)	–	–	–	0.0055	0.004–0.007	–		
Protein-bound iodine								
(1) Adults (men and women)				0.0051	0.0031–0.0071	0.001	(1) BARKER et al., <i>J. clin. Invest.</i> , 30 , 55, 1951; HARSCHA, W. H., <i>Amer. J. med. Sci.</i> , 221 , 626, 1951; SALTER and ROSENBLUM, <i>J. Endocr.</i> , 7 , 180, 1951 (method using 0.5 ml serum). – (2) TUCKER and KEYS, <i>J. clin. Invest.</i> , 30 , 869, 1951.	
(2) Men aged 18–25	–	–	–	0.00624	0.00332–0.00916	0.00146		
(2) Men aged 45–56	–	–	–	0.00563	0.00321–0.00805	0.00121		
(2) Men aged 18–56	–	–	–	0.00583	0.00319–0.00847	0.00132		

Protein-bound iodine in relation to age, basal metabolism and total cholesterol

Age	Protein-bound iodine in mg/100 ml plasma		Basal metabolism in ml O ₂ per m ²		Total cholesterol in mg/100 ml plasma		Number of tests
	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation	
18–25 years	0.00624	0.00146	128.2	11.7	188.6	36.6	130
45–56 years	0.00563	0.00121	116.3	11.6	261.3	45.7	272
18–56 years	0.00583	0.00132	120.2	12.9	237.8	54.8	402

The above values were measured on men but may be assumed to be valid also for women. It should be noted that (1) there is a slight positive correlation ($r = + 0.113$) between the basal metabolism (O₂ consumption) and the protein-bound iodine content; differences in basal metabolism between healthy subjects are mainly dependent on factors other than the circulating protein-bound iodine; (2) middle-aged men (45–56) have a significantly lower level of protein-bound iodine in the plasma and a significantly higher total cholesterol level than younger men; (3) in middle-aged men there is a positive correlation between protein-bound iodine and cholesterol, in contrast to younger men, in which no such correlation exists. After TUCKER and KEYS, *J. clin. Invest.*, **30**, 869, 1951.

Aluminium, Al	0.015	up to 0.040	–	0.046	up to 0.088	–	KEHOE et al., <i>J. Nutr.</i> , 19 , 582, 1940.	Mainly in the serum.
Manganese, Mn	0.029	0.018–0.049	–	0.0029	up to 0.0078	–	KEHOE et al., <i>J. Nutr.</i> , 19 , 582, 1940.	Mainly in the blood corpuscles.
Tin, Sn	0.022	up to 0.040	–	0.004	up to 0.010	–	KEHOE et al., <i>J. Nutr.</i> , 19 , 579, 1940.	Mainly in the blood corpuscles.
Lead, Pb	0.029	0.018–0.049 (erythrocytes:)	–	0.0029	up to 0.0078	–	KEHOE et al., <i>J. Nutr.</i> , 19 , 579, 1940.	According to KEHOE, R. A., <i>Industrial Hygiene and Toxicology</i> (in agreement with SCHMIDT, P., <i>Über die Diagnostik der Bleivergiftung im</i>
	0.057	0.029–0.086	–	–	–	–		

Lichte moderner Forschung, Jena, 1933; BRUGSCH, *Innere Medizin*, Munich, 1948; PORTHEINE, F., *Klin. Wschr.*, **30**, 83, 1952), the upper limit of the normal range of the lead level in blood is 0.060 mg/100 ml whole blood. An increase above this level indicates an abnormal exposure to or intake of lead without recognizable pathological changes necessarily becoming immediately or later apparent. Values under 0.060 mg/100 ml are to be regarded as normal, over 0.060 as critical, 0.080 or more as dangerous. With values of over 0.080 mg/100 ml further contact with lead should be forbidden, even if there are no obvious symptoms of lead poisoning. When the lead level in blood has fallen to 0.050 mg/100 ml contact with lead may be resumed.

Normal values in mg/100 ml, unless otherwise stated
(For definition of the normal range, see footnote page 317)

	Whole blood			Plasma or serum			Methods and bibliography	Remarks
	Mean	Normal range (Mean \pm 2 σ)	Standard deviation σ	Mean	Normal range (Mean \pm 2 σ)	Standard deviation σ		
Iron, Fe								
(1) Men	—	44–56	—	—	—	—	(1) (2) SACHS et al., <i>Arch. intern. Med.</i> , 52 , 366, 1933; 55 , 227, 1935; 71 , 489, 1943; (3) CHALOUKKA and LEVERTON, <i>Fed. Proc.</i> , 10 , 377, 1951 (o-phenanthrol method); (4) BESSEY, A. O., in GYÖRGY, P., <i>Vitamin Methods</i> , New York, 1951; CARTWRIGHT et al., <i>Blood</i> , 3 , 501, 1948; DAHL, S., <i>Brit. med. J.</i> , 1 , 731, 1948; (5) SMITH et al., <i>Amer. J. clin. Path.</i> , 20 , 263, 1950.	<i>Plasma or serum:</i> in well-nourished subjects hourly variations of 0.02 to 0.03 mg are observed, so that values of over 0.06 mg/100 ml must be regarded as normal. – There is no correlation between the serum iron content and the Hb content of the blood (CHALOUKKA and LEVERTON, <i>loc. cit.</i>). – Lowered in iron-deficiency anaemia, increased in untreated macrocytic anaemia and severe hepatitis. – According to BUTZENGEIGER and LANGE, <i>Ärzt. Wschr.</i> , 7 , 250, 1952, the ratio of serum-Fe to serum-Cu is the best differential-diagnostic criterion for distinguishing between parenchymatous and obstruction jaundice. In severe hepatitis the serum-Fe is greatly increased, the serum-Cu less so, while in obstruction jaundice the converse is the case; inflammatory diseases which interfere are only those such as tuberculosis or rheumatoid arthritis in which the serum iron level is lowered.
(2) Women	—	42–48	—	—	—	—		
(3) Women aged 17–25	—	—	—	0.125	—	—		
(3) Women aged 30–40	—	—	—	0.119	—	—		
(3) Women aged 40–50	—	—	—	0.113	—	—		
(3) Women aged 50–60	—	—	—	0.122	—	—		
(3) Women aged 60–70	—	—	—	0.110	—	—		
(3) Women aged 70–80	—	—	—	0.095	—	—		
(3) Women aged 80–86	—	—	—	0.093	—	—		
(4) Men and wöwen as one group.....	—	—	—	0.105	0.04–0.21	—		
(5) Men and women as one group (measured spectrographically)	—	—	—	0.068	0.018–0.118	0.025		
Copper, Cu								
	0.094	0.073–0.115	—	0.1186	0.1162–0.1210	0.0012	CARTWRIGHT et al., <i>Blood</i> , 3 , 501, 1948 (trichloroacetic acid method).	Cf. Iron. – The increase of the plasma Cu level is the largest percentage change which occurs among the blood constituents in pregnancy (GOLDSMITH, G. A., <i>Amer. J. med. Sci.</i> , 215 , 182, 1948).
Zinc, Zn								
	0.880	0.488–1.272 (erythrocytes:)	—	0.300	0–0.613	—	VALLEE and GIBSON, <i>J. biol. Chem.</i> , 176 , 445, 1948; HOCH and VALLEE, <i>ibid.</i> , 181 , 295, 1949.	
	1.440	0.911–1.969 (in 10 ⁸ leucocytes:)	—	—	—	—		
	0.0032	—	—	—	—	—		

Blood gases (see the opposite page)

Oxygen capacity

The oxygen capacity is the O₂ content of blood saturated with O₂; it consists of two fractions, the chemically combined (with haemoglobin) and the physically dissolved O₂. Usually, however, the oxygen capacity is taken as equal to the haemoglobin-combined O₂ and is calculated instead of measured (see note 3 on the opposite page).

CO₂ capacity and related values

The CO₂ capacity is the CO₂ content of whole blood or plasma in equilibrium with CO₂ at 40 mm Hg (= partial pressure of CO₂ in alveolar air). In practice only the CO₂ capacity of plasma is determined: arterial blood is drawn with exclusion of air and allowed to stand until coagulated. The plasma is then separated and after equilibration with CO₂, the ionically bound CO₂ is liberated by weak acid and measured. All operations are carried out at 0°C and 760 mmHg.

The total CO₂ extractable from plasma so treated represents the total CO₂ capacity of the plasma and consists of two fractions, the physically dissolved and the ionically combined CO₂, known as the free and combined capacity respectively. The free capacity is identical with the carbonic acid content of the plasma. The combined capacity is usually designated the alkali reserve. The CO₂ of the alkali reserve is mainly combined as bicarbonate and is therefore also known as “bicarbonate CO₂”.

The pH of the blood is primarily dependent on the ratio of carbonic acid to bicarbonate (H₂CO₃/BHCO₃), represented by HENDERSON’s equation

[H⁺] = K[H₂CO₃]/[BHCO₃]

or by the logarithmic form of HENDERSON and HASSELBALCH

pH = pK + log [BHCO₃] – log [H₂CO₃]

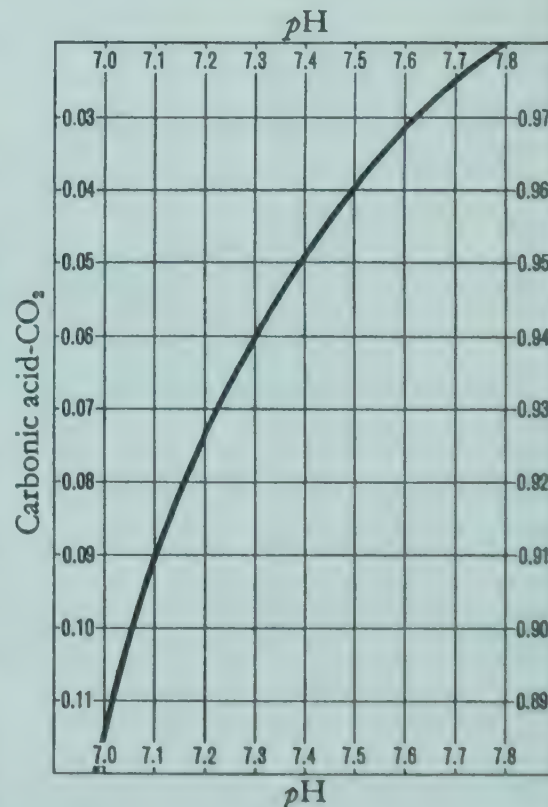
where [] indicates molar concentration, K = dissociation constant of carbonic acid, and pH = – log [H⁺], pK = – log K.

The denominator in the HENDERSON equation may be obtained with sufficient accuracy for most clinical purposes by determining the alkali reserve. For more precise measurements determination of the actual CO₂ content and pH of a blood sample under complete exclusion of air must be made. On alkalosis and acidosis, see Water and Electrolyte Balance, page 297.

The O₂ content, CO₂ content and related values relate to the actual O₂ and CO₂ content of blood (plasma) drawn and examined with complete exclusion of air. They must not be confused with the gas capacities described above, which always relate to blood (plasma) either saturated with or in equilibrium with these gases.

Diagram: pH value of blood and distribution of the total CO₂ content

Example: At pH 7.39 the total CO₂ content consists of 0.05 (5%) as carbonic acid and 0.95 (95%) as bicarbonate. With a total CO₂ content of 60 vol% and pH 7.39 for example, the blood sample therefore contains 0.05 × 60 = 3 vol% (= 1.4 mmol/l*) carbonic acid-CO₂ and 0.95 × 60 = 57 vol% (= 25.6 mmol/l*) bicarbonate-CO₂ (the latter corresponding to 25.6 mg. equiv/l* HCO₃-ions).



After SUNDERMAN and BOERNER, *Normal Values in Clinical Medicine*, Philadelphia, 1950

* Conversion factor for vol% into mmol/l (and mg. equiv/l) = 1/2.226.

Many of the values in this table* have been derived by calculation on the basis of assumed values for factors and constants, and do not have the same validity as actually measured values. Those for women are in general less well founded than those for men. Values for carbamino-CO₂ (that part of the combined CO₂ which is combined with protein), in particular, indicate order of magnitude rather than exact magnitudes. Abbreviations: M = males, F = females, art. = arterial blood, ven. = venous blood.

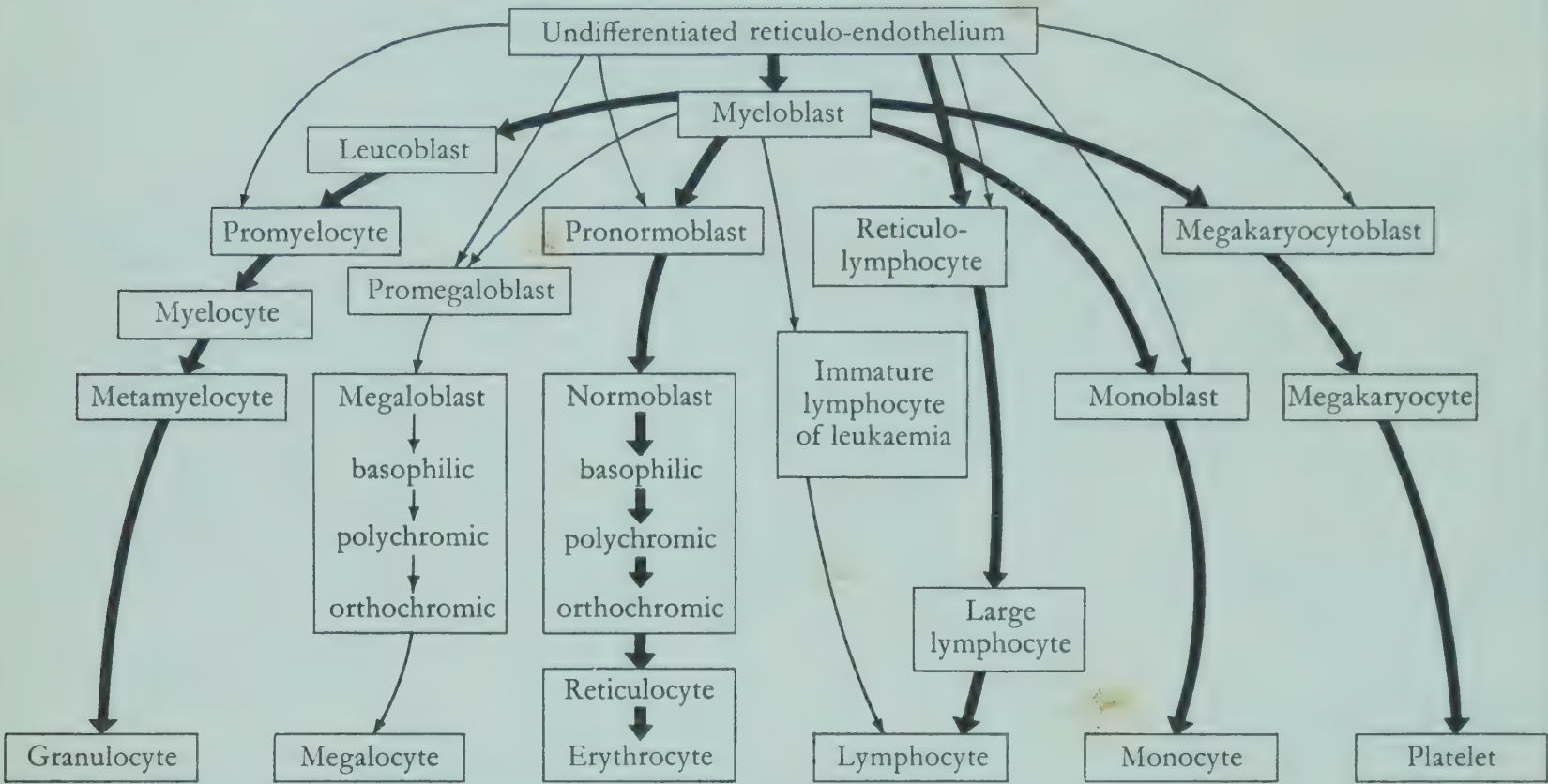
Blood gases			ml gas in 100 ml whole blood	ml gas in 45.0 ml (M) ¹ or 40.0 ml (F) ^{1,2} erythrocytes	ml gas in 55.0 ml (M) ¹ or 60.0 ml (F) ^{1,2} plasma	ml gas in 100 ml erythrocytes in contact with plasma	ml gas in 100 ml plasma in con- tact with erythrocytes	Blood gas pressure (tension) mm Hg	Factors and Constants	
Oxygen, O ₂			M	20.4 ⁴		45.3 ⁶				
1	Capacity ³	F	18.0 ^{4,5}			45.3 ⁷				
2	Content, total	art.	M	20.3 ^{8,9}	20.1	0.142	44.7	0.258	94	5.00 } Diff. art. minus 4.20 } ven. O ₂
3		F	F	17.9	17.7	0.155	44.7	0.258	94 ⁷	
4		ven. ¹⁰	M	15.3	15.2	0.060	33.9	0.110	40 ¹¹	
5			F	13.7	13.6	0.068	34.4	0.113	41 ¹¹	
6	In solution ("free" O ₂)	art.	M	0.285	0.144	0.142	0.319	0.258	94	Factor ¹² } Factor ¹³ 0.0258 ¹² } 0.02089 ¹³
7			F	0.282	0.126	0.156	0.319	0.258	94 ⁷	
8		ven. ¹⁰	M	0.122	0.061	0.061	0.136	0.110	40 ¹¹	
9			F	0.124	0.055	0.068	0.139	0.113	41 ¹¹	
10	Combined (haemoglobin-O ₂)	art.	M	20.0	20.0	0	44.4	0	94	98 } Haemoglobin-O ₂ saturation 98 } in %
11			F	17.6	17.6	0	44.4	0	94 ⁷	
12		ven. ¹⁰	M	15.2	15.2	0	33.6	0	40 ¹¹	73.5 }
13			F	13.6	13.6	0	34.3	0	41 ¹¹	
Carbon dioxide, CO ₂										
14	Capacity		M, F	43-56 ¹⁴			53-68 ¹⁴		Note: the plasma values are for plasma not in contact with erythrocytes.	
15	Free capacity (in solution)		M, F	2.7 ¹⁴			2.4-3.4 ¹⁴			
16	Combined capacity or alkali reserve (total combined CO ₂)		M, F	41-53 ¹⁴			50-65 ¹⁴ 22-30 mg. equiv HCO ₃			
17	Content, total	art.	M	49.0	16.2	32.8	36.0	59.6	41	1.217 } Factor ¹⁵ } 4.1 } Diff. art. minus 1.187 } 3.4 } ven. CO ₂ ¹⁶
18			F	48.0 ¹⁷	13.6	34.4	34.3	57.0 ¹⁷	39 ^{18,19}	
19		ven. ¹⁰	M	53.1	18.0	35.1	40.1	63.8	46.5 ¹⁹	1.201 }
20			F	51.4	14.9	36.5	37.7	60.4 ¹⁷	43 ¹⁹	
21	In solution (free CO ₂ content = carbonic acid- CO ₂)	art.	M	3.384	1.820	1.564	2.356	2.844	41	0.4399 } Factor ²⁰ } 0.5311 } Factor ²⁰ Erythro- } Plasma cytes }
22			F	2.532	0.891	1.641	2.250	2.717	39 ^{18,19}	
23		ven. ¹⁰	M	2.997	1.211	1.786	2.690	3.248	46.5 ¹⁹	0.154 }
24			F	2.785	0.965	1.820	2.437	3.013	43 ¹⁹	
25	Combined, total	art.	M	45.6	14.4	31.2	33.6	56.8	41	7.19 } pH values 7.20 } Erythro- } 7.40 cytes } 7.40 ⁷ } Plasma
26			F	45.5	12.7	32.8	32.1	54.3	39	
27		ven. ¹⁰	M	50.1	16.8	33.3	37.4	60.5 ⁸	46.5	7.17 } 7.37 ²¹ } 7.18 } 7.38 ¹⁹ }
28			F	48.7	14.0	34.7	35.3	57.4	43	
29	Carbamino-CO ₂	art.	M	2.2 ⁸	1.7	0.4	3.9	0.8	41	0.115 } Factor 0.116 } (Ery.) ²² } 0.014 } Factor Plasma ²²
30			F	1.9 ⁸	1.5	0.5	3.7	0.8	39	
31		ven. ¹⁰	M	3.1	2.6	0.5	5.8	0.8	46.5	0.154 }
32			F	2.7	2.2	0.5	5.5	0.8	43	
33	Bicarbonate-CO ₂	art.	M	43.4	12.6	30.8	29.8	56.0	41	
34			F	43.5	11.2	32.3	28.3	53.5	39	
35		ven. ¹⁰	M	47.0	14.2	32.8	31.6	59.7	46.5	
36			F	46.0	11.8	34.2	29.8	56.6	43	
Nitrogen, N ₂										
37	(in solution)	art.	M	0.979	0.494	0.484	1.099	0.881	572 ²³	Factor ²⁴ } Factor ²⁴ Erythrocytes } Plasma
38			F	0.970	0.437	0.534	1.103	0.884	574 ²³	
39		ven. ¹⁰	M	0.979	0.494	0.484	1.099	0.881	572 ²³	0.0146 } 0.0117
40			F	0.970	0.437	0.534	1.103	0.884	574 ²³	

¹ The haematocrit values used here are somewhat lower than the clinical normal values given on page 335, in part due to the rise in plasma volume in recumbent posture (v. standing). ² The exact values used for this table were 39.6 (haematocrit) and 60.4 (100 minus haematocrit = plasma per 100 ml whole blood). ³ O₂ capacity = grams Hb × 1.36. This factor is based on a Hb-Fe content of 0.339%. Cf. also note ¹. ⁴ Based on Hb contents of 15 g (M) and 13.2 g (F), both somewhat lower than the clinical values given on page 337 (cf. note ¹). ⁵ Exact value used in further calculations: 17.95. ⁶ Equivalent to 33.3 g Hb/100 ml (= 20 mmol/l) erythrocytes. ⁷ Assumed to be equal to the value for males. ⁸ Any apparent discrepancies in sums or differences are due to rounding off after calculations were made. ⁹ Average of 9 mean values from the literature = 19.5, equivalent to a Hb content of 14.34 g. ¹⁰ Mixed venous blood. ¹¹ Available mean values for mixed venous blood of males average slightly below 40, i.e. 38. ¹² Dissolved O₂ content (in ml) in 100 ml human erythrocytes = 100 × 0.0258 × O₂ pressure/760. ¹³ Dissolved O₂ content (in ml) in 100 ml (horse) plasma = 100 × 0.02089 × O₂ pressure/760. ¹⁴ See remarks on CO₂ capacity and related values on the opposite page. ¹⁵ Plasma CO₂ = F × whole-blood CO₂, F being a factor depending on pH, O₂ capacity and Hb-O₂ saturation per cent. ¹⁶ Arterio-venous CO₂ difference calculated as arterio-venous O₂ difference multiplied by the normal respiratory quotient of 0.82. ¹⁷ The blood CO₂ content in women is ca. 1 ml lower than in men (antecubital vein blood). ¹⁸ May be still lower premenstrually. ¹⁹ Calculated from the equation: pH = 6.10 + (A - k B)/k B, where pH = values in lines 25-28 (plasma column), k = plasma factor (lines 21-24) × 100/2.226 × 760, A = total CO₂ content in 100 ml plasma (in contact) × 2.226, B = CO₂ pressure. ²⁰ ml CO₂ (inc. H₂CO₃) dissolved in 100 ml erythrocytes = 0.4399 × 100 × CO₂ pressure/760. For plasma substitute 0.5311 for 0.4399. ²¹ Calculated from the arterial value for males, using the standard arterio-venous pH difference of 0.03. ²² Carbamino-CO₂ = total combined CO₂ × this factor. The values of this factor are provisional, as other factors underlying it have not yet all been determined for human blood. ²³ The arterial and venous N₂ pressures are assumed both equal to the alveolar air N₂ pressure, the latter calculated as the difference between 760 and the sum of the following: O₂ = 100; CO₂ = (M) 41, (F) 39; water vapour = 47 mm Hg. Note that the total of blood gases and water vapour varies with atmospheric pressure (normal 760 mm Hg). ²⁴ ml N₂ dissolved in 100 ml erythrocytes = 0.0146 × 100 × N₂ pressure/760. For plasma substitute 0.0117 for 0.0146.

* Lines 1-13 and 17-40 are taken from a summary based on 50 sources in ALBRITTON, E. C. (Ed.), *Standard Values in Blood*, Philadelphia, 1952, p. 120. Lines 14-16 (whole blood) are from HARRISON, G. A., *Chemical Methods in Clinical Medicine*, London, 1947, and (plasma) from GUIST, G. M., in *Mitchell-Nelson Textbook of Pediatrics*, Philadelphia, 1950, in general agreement with other authors.

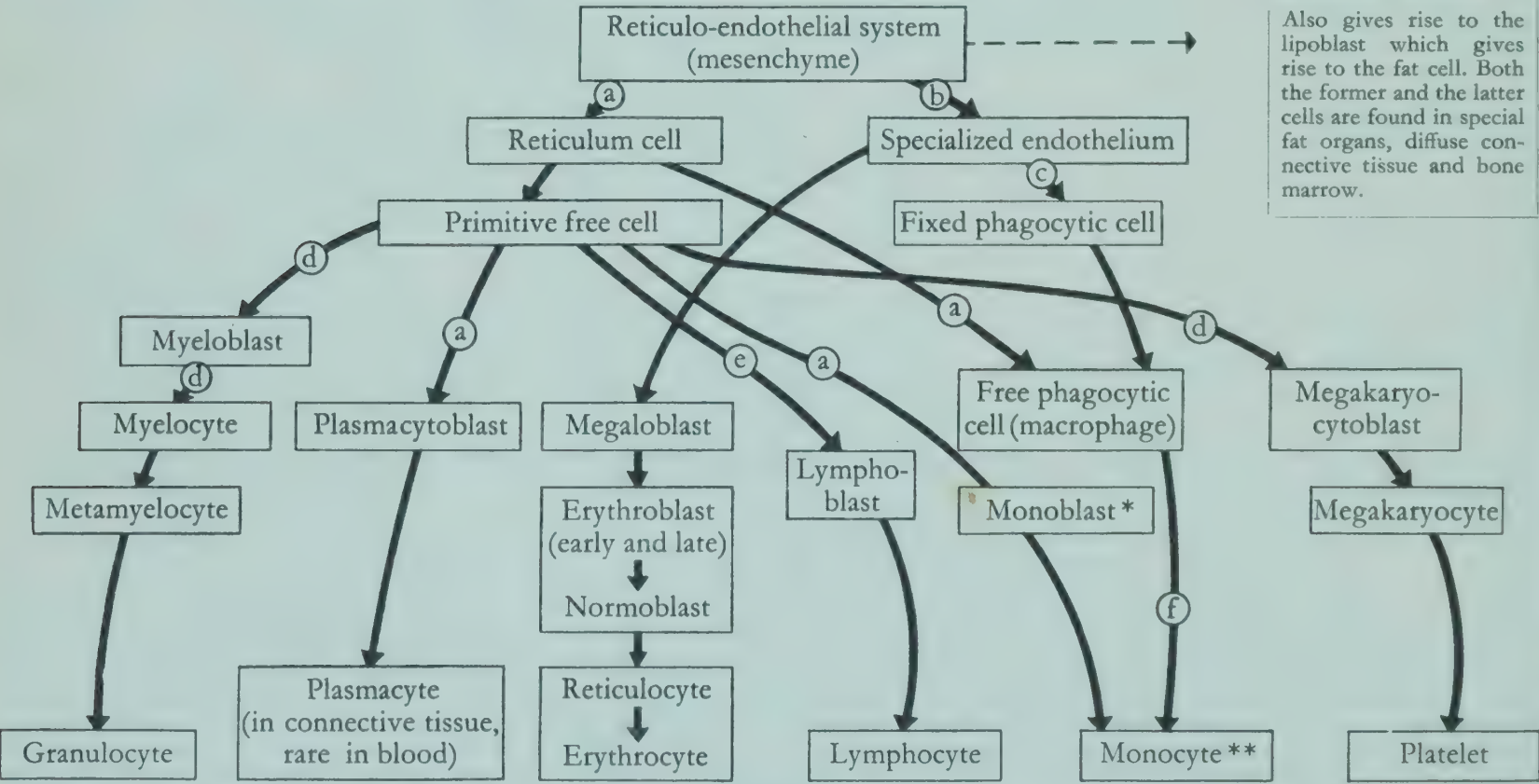
Genealogy (of the formed elements of the blood of adults)

Modified neo-unitarian (monophyletic) theory of DOWNEY, after JONES, O. P., 1952¹



Legend: The thick lines indicate the development of blood cells in the normal human adult, the thin lines the various possibilities under pathological and experimental conditions.

Polyphyletic (dualist) theory of DOAN, C. A., 1952²



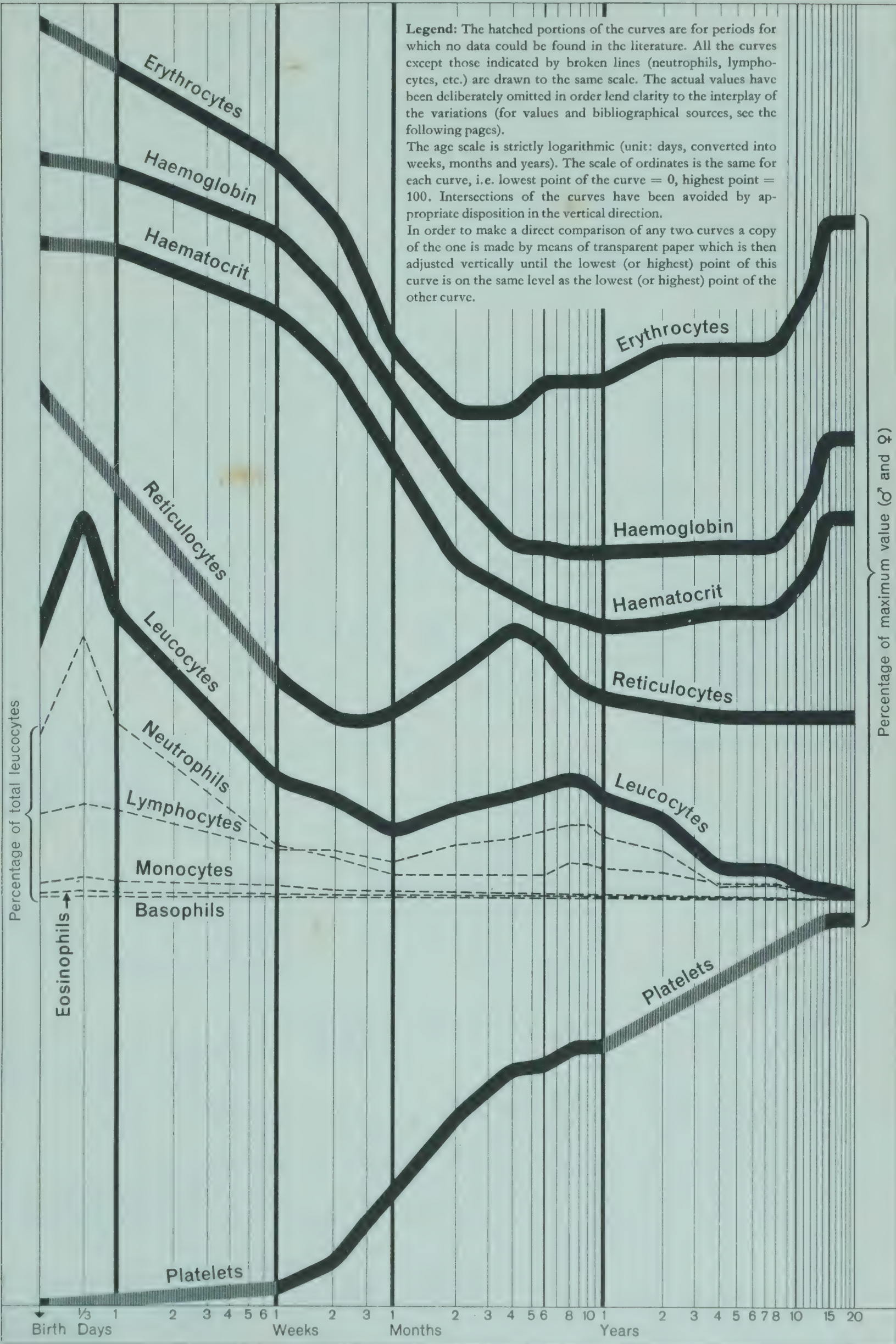
Legend: (a) In diffuse connective tissue and organ parenchyma; (b) in bone marrow, lymph nodes, spleen, KUPFFER cells of liver; (c) in lymph nodes, spleen, KUPFFER cells of liver; (d) in bone marrow; (e) in lymph nodes and spleen; (f) on demand, the macrophage may also give rise to fat cells or vice versa.

* Monoblasts may give rise to myeloblasts in tissue culture.

** Monocytes may give rise to fibroblast-like cells in tissue culture and may revert to monoblasts on demand. Monocytes may also give rise to epithelioid cells in fatty degeneration (in tuberculosis caseation) and to the LANGHANS or foreign-body giant cells.

¹) After JONES, O. P., in ALBRITTON, E. C., *Standard Values in Blood*, Philadelphia, 1952, who gives the following references: DOWNEY, H., in DOWNEY et al., *Handbook of Hematology*, New York, 1938; SUNDBERG and DOWNEY, *Amer. J. Anat.*, **70**, 455, 1942; JONES, O. P., *Arch. Path.*, **35**, 752, 1943.
²) After DOAN, C. A., in ALBRITTON, E. C., *Standard Values in Blood*, Philadelphia, 1952, who gives the following references: DOAN et al., *Contr. Embryol. Carneg. Inst.*, No. **83**, Publ. 361, Washington, 1925; CUNNINGHAM et al., *ibid.*, No. **84**, Publ. 361, 1925; DOAN, C. A., *Medicine*, **10**, 323, 1931; DOAN, C. A., *Bull. N. Y. Acad. Med.*, **15**, 668, 1939; DOAN, C. A., *J. Lab. clin. Med.*, **26**, 89, 1940.

Diagrammatic comparison of fluctuations of the formed elements during growth



Synopsis of Blood – Formed Elements – Erythrocytes
Immature Erythrocyte Forms

(For genealogy, see page 332)

Erythroblasts (as percentage of the nucleated cells)	Normal values	Methods and bibliography	Remarks
Adults	0	From DIAMOND, L. K., in <i>Mitchell-Nelson Text- book of Pediatrics</i> , Phil- adelphia, 1950.	The <i>normoblasts</i> which first appear in the blood in erythroblastosis bear a marked resemblance, except for the nucleus, to ery- throcytes in respect of shape, staining, haemoglobin content and size. Erythro- blastosis is connected (with exceptions) with increase of the erythrocytes. It is a sign, however, of a dysfunction of haematopoiesis rather than of a hyperfunction (according to HEILMEYER). – For evolution, see page 332, for morphology, etc. of erythroblasts, see the literature.
Newborn			
At birth	1–5		
2 days old	2		
Subsequently	0		

Reticulocytes

(in parts per 1000 parts erythrocytes)

Age	Mean	Normal range*			
At birth	43.5	25.0–65.0			
1 week	11.2	1.0–45.0			
2 weeks	6.7	2.0–15.0			
3 weeks	6.3	2.0–13.0			
4 weeks	7.3	1.0–10.0			
2 months	12.0	5.0–31.0			
4 months	16.6	9.0–29.4			
6 months	13.8	7.2–23.0			
8 months	11.2	6.5–19.0			
10 months	9.7	6.2–18.0			
12 months	9.0	6.0–17.0			
Men and women as one group	7.5	1.2–13.7	3.13	} Standard deviation σ	
Men	6	1.6–10.4	2.2		
Women	9	2.6–15.4	3.2		
(The difference between men and women is significant)					

son, C. J., *Arch. intern. Med.*, **86**, 797, 1950 (values for the group ♂ + ♀ corrected to a sex ratio of 1:1). *Values for children* from WASHBURN, A. H., *Amer. J. Dis. Child.*, **62**, 530, 1941, and DE CHASTONAY, E., *Helv. paediat. Acta*, **6**, 257, 1951.

reticulum under vital staining. Usually somewhat larger than the average erythrocyte and more resistant to haemolysis. There is an average difference of 3‰ between men and women. Increased in blood regeneration during the reparative phase of anaemia. – An abrupt increase of 4% up to 40% indicates a reticulocytic crisis, e.g. after starting treatment of pernicious or severe hypochromic anaemia (according to SCHULTEN). – The number of reticulocytes in the blood is usually a measure of the blood regeneration activity. For the relation between the number of reticulocytes and the erythrocyte coproporphyrin, see page 338. – For comparison between the variation in the reticulocyte count and other blood values, see the previous page. – Physiologically higher count in children, permanent pathological increase (up to 20%) in congenital haemolytic jaundice.

Polychromatic erythrocytes	Staining with basic dyes.	<i>Polychromatophilia</i> = appearance of diffuse bluish colour, varying in intensity from ery- throcyte to erythrocyte, on staining with basic dyes. It parallels reticulation and like the latter is a sign of increased regeneration. Polychromatic erythrocytes are mostly macrocytes.
----------------------------------	---------------------------	--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Basophilic granulated erythrocytes	As above	Likewise a sign of increased (but degener- ative) regeneration: in adults basophilic stippling is not a normal stage in the development of the erythrocytes like reti- culation and polychromatophilia and does not run at all parallel with these. Occurs mainly in and after lead poisoning.
------------------------------------------	----------------	------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Inclusion bodies

HEINZ bodies	Vital staining	On staining with Nile blue sulphate appear as blue granules on the edge of the erythro- cyte, more rarely in the middle. HEINZ bodies are observed in poisoning (aniline, phenyl- hydrazine, sulphonamides, etc.) and fre- quently also after splenectomy.
--------------------	----------------------	---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

HOWELL-JOLLY bodies	Staining with nuclear stains	Granules of diameter 1–2 μm, staining deep- ly with nuclear stains, observed occasionally in erythrocytes. Very probably of nuclear derivation. – Appear occasionally (very few) in anaemia, in large numbers after splen- ectomy.
---------------------------	---------------------------------	---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

CABOT's rings		Threadlike rings and convolutions in the erythrocytes of haemopathic patients. Oc- cur occasionally in conjunction with poly- chromatophilia and HOWELL-JOLLY bodies. Very probably nuclear membrane remnants.
---------------------	--	----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

* See footnote page 317.

(See also pages 332 and 333)

Erythrocytes	Mean	Normal range*	Standard dev. σ	Methods and bibliography	Remarks
Specific gravity ($\frac{25}{4}^{\circ}\text{C}$)	1.0983	1.095–1.101	—	VAN SLYKE et al., <i>J. biol. Chem.</i> , 183 , 305, 1950; GREGERSEN and SCHIRO, <i>Amer. J. Physiol.</i> , 121 , 284, 1938.	The specific gravity of whole blood is dependent mainly on the relatively high specific gravity of the erythrocytes. Cf. specific gravity of blood and plasma and haemoglobin content of erythrocytes. — With a water content of 60–67% the erythrocytes are among the “driest” cells of the organism.
Hydrogen-ion concentration	pH7.24	pH 7.21–7.26	—	GRAM, A. C., <i>Amer. J. med. Sci.</i> , 168 , 521, 1924.	
Lifetime (days)					
Men and women as one group	115	—	—	LONDON et al., <i>J. biol. Chem.</i> , 179 , 463, 1949; CALLENDER et al., <i>J. Path. Bact.</i> , 57 , 129, 1945.	Determined by means of glycine tagged with radioactive ^{15}N . Corresponds to an erythrocyte replacement rate of ca. 0.9% per day.
Men	120	—	—		
Women	109	—	—		

For further physical and chemical data, see pages 305, 306, 309, 310, 317, 318, 323–327, 329, 330.

Erythrocyte count (Red blood count, RBC) (in millions per cubic millimetre of peripheral venous blood)				Values from MERRITT and DAVIDSON, <i>Amer. J. Dis. Child.</i> , 46 , 991, 1000, 1001, 1008, 1933; GUEST et al., <i>ibid.</i> , 56 , 529, 1938; GUEST, G. M., <i>Nutrition: Newer Diagnostic Methods</i> , 16. Conf. Milbank Memorial Fund, 1938; DE MARSH et al., <i>J. Amer. med. Ass.</i> , 116 , 2568, 1941; DE MARSH et al., <i>Amer. J. Dis. Child.</i> , 75 , 860, 1948; MCBEE et al., <i>J. Nutr.</i> , 42 , 539, 1950; WATSON, C. J., <i>Arch. intern. Med.</i> , 86 , 797, 1950; DIAMOND, L. K., in <i>Mitchell-Nelson Textbook of Pediatrics</i> , Philadelphia, 1950; WINTROBE, M. M., <i>Clinical Hematology</i> , Philadelphia, 1952.	<i>Newborn</i> (1 week): The erythrocyte count of the cutaneous (capillary) blood is greater than that of the blood of the sagittal sinus. — If the umbilical cord is not tied until after the expulsion of the placenta the erythrocyte count is ca. 560,000/mm ³ greater than if the cord is tied immediately after the birth. <i>Physiologically increased</i> in acclimatization to high altitudes. — Measurements made with the aid of ^{32}P -tagged erythrocytes have given markedly lower figures for the total erythrocytes circulating in the body than those calculated from counts of peripheral venous blood. — The erythrocyte concentration in peripheral venous blood is only diagnostically reliable when used in conjunction with a measurement of the total blood volume: an increase in the latter, for example, can increase the total number of erythrocytes in the body (polycythaemia) while the concentration in peripheral venous blood nevertheless remains normal. In hydraemia, on the other hand, a subnormal erythrocyte concentration in peripheral venous blood may be accompanied by a normal total of erythrocytes in the body.
Age					
At birth (see remarks)	5.7	4.8 – 7.1	—		
1 day	5.6	4.7 – 7.0	—		
1 week	5.3	4.5 – 6.4	—		
2 weeks	5.1	4.3 – 6.0	—		
3 weeks	4.9	4.1 – 6.0	—		
4 weeks	4.7	3.9 – 5.9	—		
2 months	4.5	3.8 – 5.8	—		
4 months	4.5	3.8 – 5.3	—		
6 months	4.6	3.9 – 5.3	—		
8 months	4.6	4.0 – 5.4	—		
12 months	4.6	4.0 – 5.5	—		
2– 8 years	4.7	3.8 – 5.4	—		
9–13 years	4.89	3.73– 6.05	0.58		
Men and women as one group	5.10	4.3 – 5.9	0.40		
Men	5.43	5.1 – 5.77	0.17		
Women	4.77	4.3 – 5.25	0.28		
Haematocrit value (Packed cell volume, PCV) (= volume percentage of erythrocytes in peripheral venous blood)					

Age				By centrifuging; by calculation from specific gravities of whole blood and plasma.—Values from GUEST, G. M. (1938), <i>loc. cit.</i> ; DIAMOND, L. K. (1950), <i>loc. cit.</i> ; MCBEE et al. (1950), <i>loc. cit.</i> ; WATSON, C. J. (1950), <i>loc. cit.</i> ; GLASER, K.; in ALBRITTON, E. C., <i>Normal Values in Blood</i> , Philadelphia, 1952; WINTROBE, M. M. (1952), <i>loc. cit.</i>	The haematocrit value or packed cell volume is primarily dependent on the erythrocyte concentration, so that the above considerations equally apply. It is also affected by the shape and size of the erythrocytes. This purely relative nature of the haematocrit value must be borne in mind when the value is applied diagnostically.
At birth	56.6	—	—		
1 day	56.1	—	—		
1 week	52.7	—	—		
2 weeks	49.6	—	—		
3 weeks	46.6	—	—		
4 weeks	44.6	—	—		
2 months	38.9	—	—		
4 months	36.5	—	—		
6 months	36.2	—	—		
8 months	35.8	—	—		
10 months	35.5	—	—		
12 months	35.2	—	—		
2 years	35.5	—	—		
4 years	37.1	—	—		
6 years	37.9	—	—		
9–13 years	41.3	32.3–50.3	4.52		
Men and women as one group	43.3	36.5–50.3	3.46		
Men	46.2	43.2–49.2	1.5		
Women	40.6	35.8–45.4	2.4		

Mean corpuscular volume, MCV (in cubic micrometres, μm ³)				PCV (in ml/100 ml blood) × 10/RBC (in millions/mm ³) = MCV (in μm ³). <i>Adult values</i> from WHITBY and BRITTON, <i>Disorders of Blood</i> , London, 1935; and MCBEE et al., <i>loc. cit.</i> , 1950. <i>Values for children</i> from GLASER, K. (1951), <i>loc. cit.</i> ; WINTROBE, M. M. (1952), <i>loc. cit.</i>	The mean corpuscular (erythrocyte) volume may be regarded as an absolute value. The only factor which could militate against this is the shape of the erythrocytes and this is unlikely in view of the plasticity of the cells and the high pressure exerted on them in the haematocrit.
Adults	85	78–94	—		
Children					

Age	Mean	Age	Mean	Age	Mean
At birth	106	2 months	85	2 years	78
1 day	106	4 months	79	4 years	80
1 week	101	6 months	78	6 years	80
2 weeks	96	8 months	77	8 years	80
3 weeks	93	10 months	77	10 years	80
4 weeks	91	12 months	77	12 years	81

* See footnote page 317.

Erythrocytes	Mean	Normal range*	Standard dev. σ	Methods, bibliography, remarks
Mean diameter (in micrometres, μm)				Determination: Direct microscopic measurement.
Age				Values for children from DIAMOND, L. K., in <i>Mitchell-Nelson Textbook of Pediatrics</i> , Philadelphia, 1950.
At birth	—	8–9	—	Adult values from PRICE-JONES, C., <i>Red Blood Cell Diameter</i> , London, 1933.
1 month	~ 7	—	—	Remarks: Size distribution of erythrocytes: <i>normocytes</i> , 6.5–8.5; <i>microcytes</i> , under 5; <i>macrocytes</i> , over 10. – Predominance of either of the latter sizes is known respectively as <i>micro-</i> and <i>macro-cytosis</i> . The standard deviation of the erythrocyte diameter is a measure of the <i>anisocytosis</i> , i.e. the degree of exaggeration of the usual size variation. For calculation of the standard deviation, see page 32.
2 months	~ 6	—	—	<i>Microcytosis</i> (without marked anisocytosis) occurs particularly in compensated haemolytic jaundice, <i>macrocytosis</i> (without marked anisocytosis) appears relatively rapidly in liver diseases (mean value in infectious hepatitis 8.15, σ 0.64; in cirrhosis of the liver 8.45, σ 0.66) without increase of poikilocytes; in pernicious anaemia; in vitamin-B ₁ deficiency (after LÜDIN, H., <i>Helv. med. Acta</i> 4/5, 340, 1950). <i>Pronounced anisocytosis</i> occurs above all in iron-deficiency anaemia.
3–3½ months	~ 5	—	—	The diminution of the erythrocyte diameter, in conjunction with the parallel reduction in haemoglobin content, causes a physiological <i>microcytosis</i> combined with <i>hypochromia</i> in infants of 3–3½ months, a condition which is normalized by the 7th month.
5 months	~ 6	—	—	Determination: $\epsilon = \sqrt{1 - (b/a)^2}$ (a = greatest diameter, b = smallest diameter).
8 months	~ 7	—	—	Values from ŽINI and LEUBNER, <i>Schweiz. med. Wschr.</i> , 16, 382, 1951.
Adults	7.202	6.858–7.546	0.172	Remarks: Predominance of oval forms: <i>elliptocytosis</i> .
Numerical eccentricity ϵ				<i>Constitutional elliptocytosis</i> (very rare; 0.04%; harmless) is characterized by elliptocytes of uniform shape.
Percentage of erythrocytes				<i>Symptomatic elliptocytosis</i> with non-uniform elliptocytes and combined with a parallel increase in poikilocytes occurs in many diseases which are accompanied by blood changes (Hb., erythrocyte count, displacement of the PRICE-JONES curve), particularly in pernicious anaemia and leukaemia, but also in pulmonary tuberculosis, for example. Symptomatic elliptocytosis is of value prognostically and in assessment of the course of a disease, since it is only normalized on complete return to health (after ŽINI and LEUBNER, <i>loc. cit.</i>).
82 %	0.00	—	—	<i>Poikilocytosis</i> , in which there is complete irregularity of erythrocyte form, is very probably due to abnormal deformability (cf. symptomatic elliptocytosis, above).
9.2 %	0.01	—	—	<i>Sickle cells</i> present a special form of poikilocytosis and are found almost exclusively in negroes or in individuals whose blood contains an admixture of negro blood (ca. 10% of negroes show the sickling trait). Their presence is usually but not always associated with a form of hereditary chronic haemolytic anaemia known as <i>sickle-cell</i> or <i>drepanocytic anaemia</i> .
8.2 %	—	0.71–0.80	—	Determination: (1) direct microscopic measurement, (2) assuming that erythrocytes have a cylindrical form, by dividing the mean corpuscular volume by the product ($\pi \times$ square of ½ the mean erythrocyte diameter).
0.3 %	—	0.81–0.90	—	Remarks: <i>Spherocytes</i> have a greater thickness, i.e. a more spherical form (after NAEGELI). <i>Spherocytosis</i> is usually a sign of lowered osmotic resistance of the erythrocytes (spherocytes are intermediate in shape between normal and haemolyzed erythrocytes) and therefore appears in pronounced form in haemolysis (in 5% NaCl solution the erythrocytes are mostly complete spherical with thickness and diameter of ca. 4–5 μm , the volume thus remaining fairly constant. – After DAMESHEK, W., <i>Hemolytic Mechanisms</i> , in <i>Blood</i> , Special Issue No. 2, 43, 1948).
0.2 %	—	0.91–0.98	—	Values from WINTROBE, M. M., <i>Clinical Hematology</i> , Philadelphia, 1952.
Thickness (1)	—	1.5–1.6	—	Remarks: The average total surface area of the erythrocytes in the human body amounts to ca. 3820 sq. metres, or 2000 times the surface area of the body.
(in micrometres, μm) (2)	~ 2.1	—	—	
Surface area	~ 140	—	—	
(in square micrometres, μm^2)				

* See footnote page 317.

(See also page 333)

Erythrocytes

Haemoglobin content

(in grams per 100 ml of peripheral venous blood)

Age

	Mean	Normal range*	Standard dev. σ
At birth	21.5	18.0–27.0	—
1 day	21.2	17.7–26.5	—
1 week	19.6	16.2–25.5	—
2 weeks	18.0	14.5–24.2	—
3 weeks	16.6	13.2–23.0	—
4 weeks	15.6	12.0–21.8	—
2 months	13.3	10.8–18.0	—
4 months	12.4	10.2–15.0	—
6 months	12.3	10.0–15.0	—
8 months	12.1	9.8–15.0	—
10 months	11.9	8.4–14.9	—
12 months	11.6	9.0–14.6	—
2 years	11.7	9.2–15.5	—
4 years	12.6	9.6–15.5	—
6 years	12.7	10.0–15.5	—
8 years	12.9	10.3–15.5	—
9–13 years	13.1	10.8–15.4	1.14
Men and women as one group	14.35	12–17	1.38
Men	15.4	13.6–17.2	0.90
Women	13.3	11.5–15.0	0.89

Methods, bibliography, remarks

Determination: By haemometer (colorimetrically), spectrometrically, from the O₂-combining capacity, from the Fe content, from specific gravities *of plasma and serum. – Values are from the sources listed under erythrocyte count (page 335).

Remarks: *Newborn* (1 week): the haemoglobin content of the cutaneous (capillary) blood is greater than that of the blood of the sagittal sinus. – If the umbilical cord is not tied until after the expulsion of the placenta the haemoglobin content is ca. 2.6 g/100 ml greater than if the cord is tied immediately after the birth.

The haemoglobin content of blood is primarily a function of the erythrocyte concentration and thus rises and falls with the erythrocyte count. – Since the structure of Hb is not known present methods of determination depend on the use of empirical factors, for example that 1 gram Hb combines with 1.34 ccm O₂ or that 1 gram Hb contains 0.335% Fe. These factors were originally obtained from measurements on Hb from other species. More recent determinations by BERNHART and SKEGGS, *J. biol. Chem.*, **147**, 19, 1943, on human Hb have given values of 1.36 ccm O₂ and 0.340% Fe per gram Hb. Values for Hb content measured with the aid of the earlier factors are therefore presumably ca. 1.5% too high.

Determination of haemoglobin by haemoglobinometer

Clinical haemoglobinometers are based on various norms and on practical grounds must be read before breakdown of the haemoglobin takes place. Data on Hb content given in the literature are derived from the use of a variety of haemoglobinometers and are thus only to a limited extent comparable, and then only when the method, including the reading time, is clearly laid down. – The determination of Hb from the specific gravities of blood and plasma usually gives more comparable values, not because the method itself is more accurate but because it involves less specific and subjective sources of error (cf. specific gravity, page 304).

Mean corpuscular haemoglobin (MCH or HbE) content

(in micromicrograms, μμg = 10⁻¹² gram)

Mean	Normal range	
29	27.4–35.0	(at sea level)
—	30.2–35.8	(at 3730 m)
—	28.9–38.9	(at 4540 m)
		(men and women, for children see below)

Determination: (Haemoglobin in g/100 ml blood divided by erythrocyte count in millions per cubic millimetre) × 10 (see adjacent nomogram).

Values from HURTADO et al., *Arch. intern. Med.*, **75**, 284, 1945.

Remarks: Haemoglobin contents below, above and within the normal range are denoted respectively as hypo-, hyper- and normo-chromic. The mean corpuscular (erythrocyte) haemoglobin content provides a reliable and comparable measure of hypo-, normo- and hyper-chromia.

The so-called **Colour Index** (= Hb content as % of normal divided by erythrocyte count as % of normal) should give the same information but does so only when (1) separate norms are used for men and women, and (2) when the norms for Hb content and erythrocyte count are in the relation 15.8:5. Colour index data in the literature are only comparable when they have been calculated on a uniform basis and in accordance with a clearly defined method. Expression of the mean corpuscular haemoglobin in micromicrograms is therefore much to be preferred and renders the colour index superfluous.

Mean corpuscular haemoglobin concentration (MCHC)

(in grams per 100 ml erythrocytes = %)

Mean	Normal range	
33.5	31.3–39.6	(at sea level)
—	33.0–36.6	(at 3730 m)
—	32.7–36.7	(at 4540 m)
		(men and women, for children see below)

Determination: (Haemoglobin in g/100 ml blood divided by haematocrit value) × 100.

Values from HURTADO et al., *Arch. intern. Med.*, **75**, 284, 1945.

Mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration in adolescence

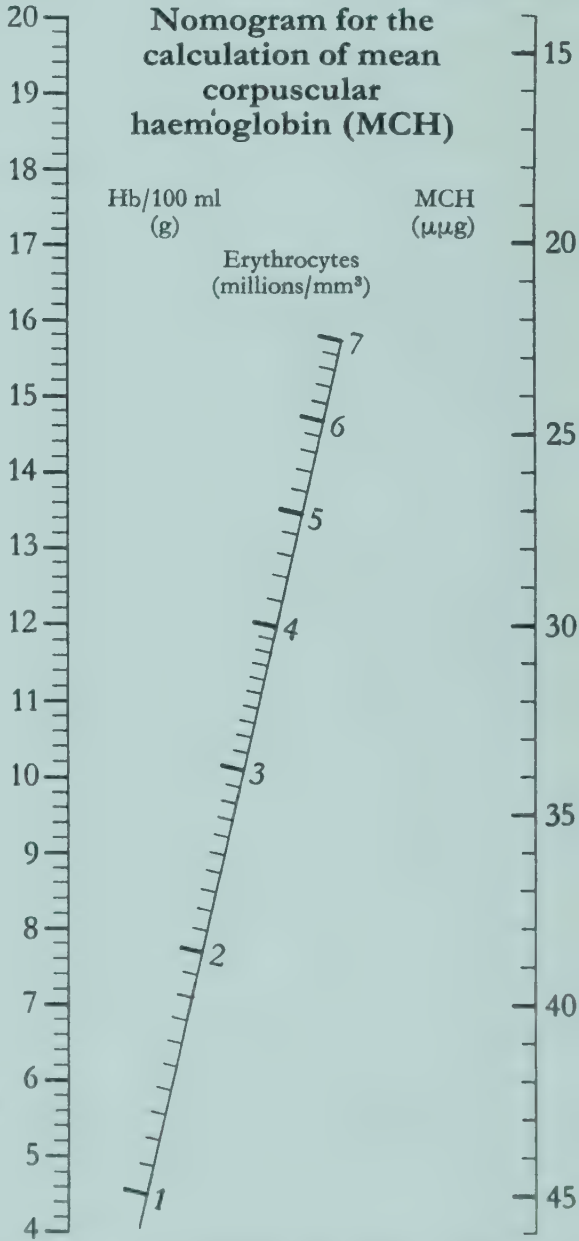
Age	MCH (μμg)	MCHC %	Age	MCH (μμg)	MCHC %
At birth	38	38	8 months	26	33.8
1 day	38	37.8	10 months	26	33.5
1 week	37	37.2	12 months	25	33.0
2 weeks	35	36.3	2 years	25	33.0
3 weeks	34	35.6	4 years	27	34.0
4 weeks	33	35.0	6 years	27	33.5
2 months	30	34.2	8 years	27	33.2
4 months	27	34.0	10 years	27	33.3
6 months	27	34.0	12 years	28	33.8

Haemoglobin content of plasma

0–0.5 mg/100 ml (men and women)

Determination: spectrometrically.

Remarks: Increased in all kinds of haemolysis. The renal threshold value for Hb in serum is ca. 150 mg/100 ml, so that pronounced haemoglobinaemia is possible without necessarily resulting in haemoglobinuria.



A line is drawn connecting the measured haemoglobin content (left-hand scale) with the measured erythrocyte count (middle scale). The intersection of this line with the right-hand scale gives the mean corpuscular haemoglobin.

* See footnote page 317.

Erythrocytes	Mean	Normal range*	Standard dev. σ	Methods and bibliography	Remarks
Carboxyhaemoglobin (as percentage of the haemoglobin)	3.4	0.0–8.2	2.4	After VAN SLYKE et al., <i>J. biol. Chem.</i> , 166 , 121, 1946.	Determined photometrically with KCN immediately after drawing of the venous blood sample.
Expressed as volume per cent of CO in whole blood	0.15	0.05–0.25	0.05	After PACE et al., <i>Amer. J. Physiol.</i> , 147 , 352, 1946	Measured on 32 healthy naval ratings between the ages of 18 and 42.
Methaemoglobin (Haemiglobin, ferrihaemoglobin, as per cent of the haemoglobin)	0.4	0.0–1.1	—	After EVERETT, M. R., <i>Medical Biochemistry</i> , New York, 1946.	
Protoporphyrin III (in micrograms per 100 ml erythrocytes)				The protoporphyrin content of the erythrocytes is not so closely correlated with the reticulocyte count as is the case with coproporphyrin. The protoporphyrin content is slightly increased in haemolytic anaemia (60–120 μg), greatly increased in iron-deficiency anaemia (180–390 μg) and has the highest values in lead poisoning (200–1300 μg). Values are normal in pernicious anaemia (after WATSON, <i>loc. cit.</i>).
Men and women as one group ..	36.4	19–53	8.5	WATSON, C. J., <i>Arch. intern. Med.</i> , 86 , 797, 1950 (Values ♂ + ♀ as one group corrected to a sex ratio of 1:1).	Contrary to earlier belief (VAN DEN BERGH et al., <i>Klin. Wschr.</i> , 11 , 1534, 1932) it is now considered highly probable that coproporphyrin is a precursor and not a breakdown product of haemoglobin-porphyrin. The coproporphyrin content is closely correlated with the reticulocyte count and is highest in diseases involving retarded haemoglobin synthesis, such as iron-deficiency anaemia (180–390 μg) and lead poisoning (up to 4000 μg). It is slightly increased in haemolytic anaemia. Zero in pernicious anaemia, it increases with the reticulocyte count, but more rapidly, after treatment with vitamin B ₁₂ (after WATSON, <i>loc. cit.</i>). – The urinary excretion of coproporphyrin III is not correlated with the coproporphyrin content of the erythrocytes.
Men } Sex difference	28.5	19.5–37.5	4.5		
Women } very significant	41.7	30–53.5	5.9		
Coproporphyrin III (in micrograms per 100 ml erythrocytes)					
Men and women as one group ..	0.5	0–1.6	0.54	After WATSON, 1950, <i>loc. cit.</i>	
Men	0.3	0–1.1	0.39		
Women	0.7	0–1.9	0.6		
Verdohaemoglobin (as per cent of the haemoglobin)	—	5–8	—	BARKAN and WALKER, <i>J. biol. Chem.</i> , 131 , 447, 1939; HAVEMANN, R., <i>Klin. Wschr.</i> , 20 , No. 21, 1941.	

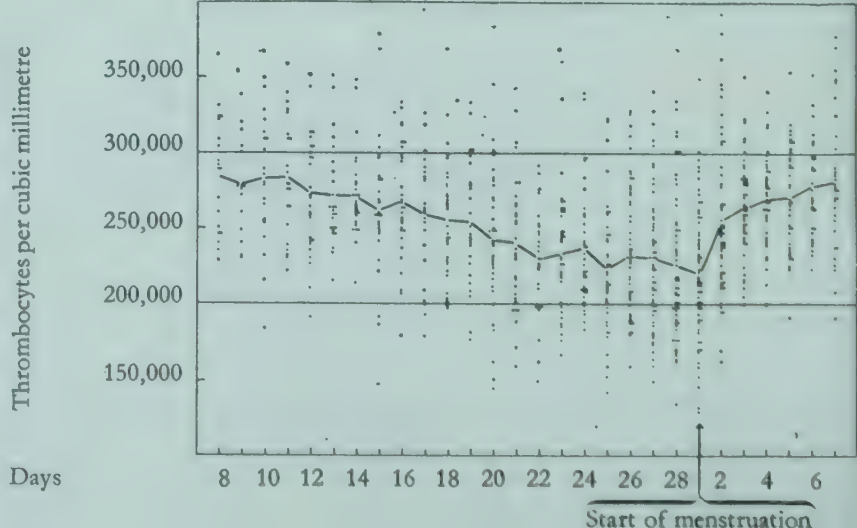
Thrombocytes (Platelets; for genealogy, see page 332; for thrombocytes and other blood values in adolescence, see page 333)

Thrombocyte count (in thousands per cubic millimetre whole blood)					
Cutaneous blood					
Age					
At birth	227	140–290	—	Direct method of WOOD et al.; values from MERRITT and DAVIDSON, <i>Amer. J. Dis. Child.</i> , 46 , 991, 1000, 1001, 1008, 1933.	The number of platelets is ca. 15% higher in venous blood than in cutaneous blood, and ca. 12% higher in arterial blood than in venous blood. In women the platelet count falls before menstruation, then rises again afterwards (see diagram). After the age of 60 the number of platelets is markedly less than in youth. The platelet count and distribution are furthermore dependent on physical constitution, physical exertion, altitude and environmental temperature.
1 week	235	150–320	—		
2 weeks	247	163–340	—		
3 weeks	267	177–367	—		
4 weeks	280	185–390	—		
2 months	315	200–428	—		
4 months	338	205–465	—		
6 months	340	205–470	—		
8 months	345	210–473	—		
10 months	345	212–470	—		
12 months	345	218–470	—		
Adults	—	273–545	—	Direct method. Values from AGGLER, HOWARD and LUCIA, <i>Blood</i> , 1 , 472, 1946.	
Adults	—	133–367	—	Direct method. Values from TOCANTINS, L. M., <i>Medicine</i> , 17 , 155, 1938.	
Adults	—	500–900	—	Indirect method. Values from DAMESHEK, W., <i>Arch. intern. Med.</i> , 50 , 579, 1932.	
Venous blood	—	88–532	—	Direct method. Values from TOCANTINS, <i>loc. cit.</i>	

Diameter (in micrometres, μm)		
13–18% of thrombocytes	1.8	—
72% of thrombocytes	2.3	—
9–10% of thrombocytes	3.6	—

Volume (in cubic micrometres, μm ³)		
After VAN ALLEN, <i>Münch. med. Wschr.</i> , 74 , 141, 1927	0.49	0.35–0.56
After HORWITZ, S., <i>Klin. Wschr.</i> , 10 , 1613, 1931	—	2.5–7.5
After TOCANTINS, L. M., <i>Medicine</i> , 17 , 155, 1938	—	10–12

Thrombocyte count during the menstrual cycle
After POHLE, F. J., *Amer. J. med. Sci.*, **197**, 40, 1939



* See footnote page 317.

(See also pages 332 and 333)

Variation with age of the leucocyte count and distribution

Age	Total leucocytes	Neutrophils		Eosinophils		Basophils		Lymphocytes		Monocytes		Neutrophilic myelocytes	
	Number per mm ³	Number per mm ³	%	Number per mm ³	%	Number per mm ³	%	Number per mm ³	%	Number per mm ³	%	Number per mm ³	%
1 day ¹	15,250-45,000	8623-33,525	53-82.5	0- 895	0-6	76-636	0-4	2000-8722	5-56	696-5175	15-34	0- 1908	0-13
3-5 days ¹	4000-18,800	1800-10,152	32-59	168-1110	1.5-13	0-215	0-2	600-5184	15-44.5	920-4324	10-23	0- 174	0- 1.5
6-8 days ¹	7600-16,400	2156- 8528	26.5-67	160- 727	1.5-7	0-196	0-1	1292-7015	17-61	760-2362	7-19.5	0- 437	0- 3
9-11 days ¹	8100-16,500	1976- 6141	18.5-46	205- 873	1.5-6.5	0-269	0-2	2937-9453	22-69	1164-3738	8.5-28	0- 102	0- 1
3 months to 3 years ² ...	6050-17,450	2000- 7000	40-50	25- 700	0.5-5	0- 50	0-0.5	4000-9000	50-60	25- 700	0.5-5	-	-
3-5 years ²	5575-15,450	3000- 8000	50-60	50- 700	1-5	0- 50	0-0.5	2500-6000	40-50	25- 700	0.5-5	-	-
5-15 years ³	4575-12,650	3000- 7000	55-65	50- 500	1-5	0- 50	0-0.5	1500-4500	30-40	25- 600	0.5-6	-	-
Adults ³	5000-10,000	3000- 7000	60-70	50- 400	1-4	0- 50	0-1	1000-3000	20-30	100- 600	2-6	-	-
Adults, mean	7000	4500	66	100	1.5	25	0.5	1800	26	450	6	-	-

Eosinophils

The percentage fall in eosinophils after corticotropin injection provides a test (specific when positive) for the evaluation of adrenocortical function (THORN's test, see page 189). There is no correlation between the number of circulating eosinophils and the number of circulating leucocytes.

Normal values⁴:

Fasting :

8 a.m. 20-880
mean 221

12 noon 10-790
mean 171.5

Clinical norm 25-300 (fasting)

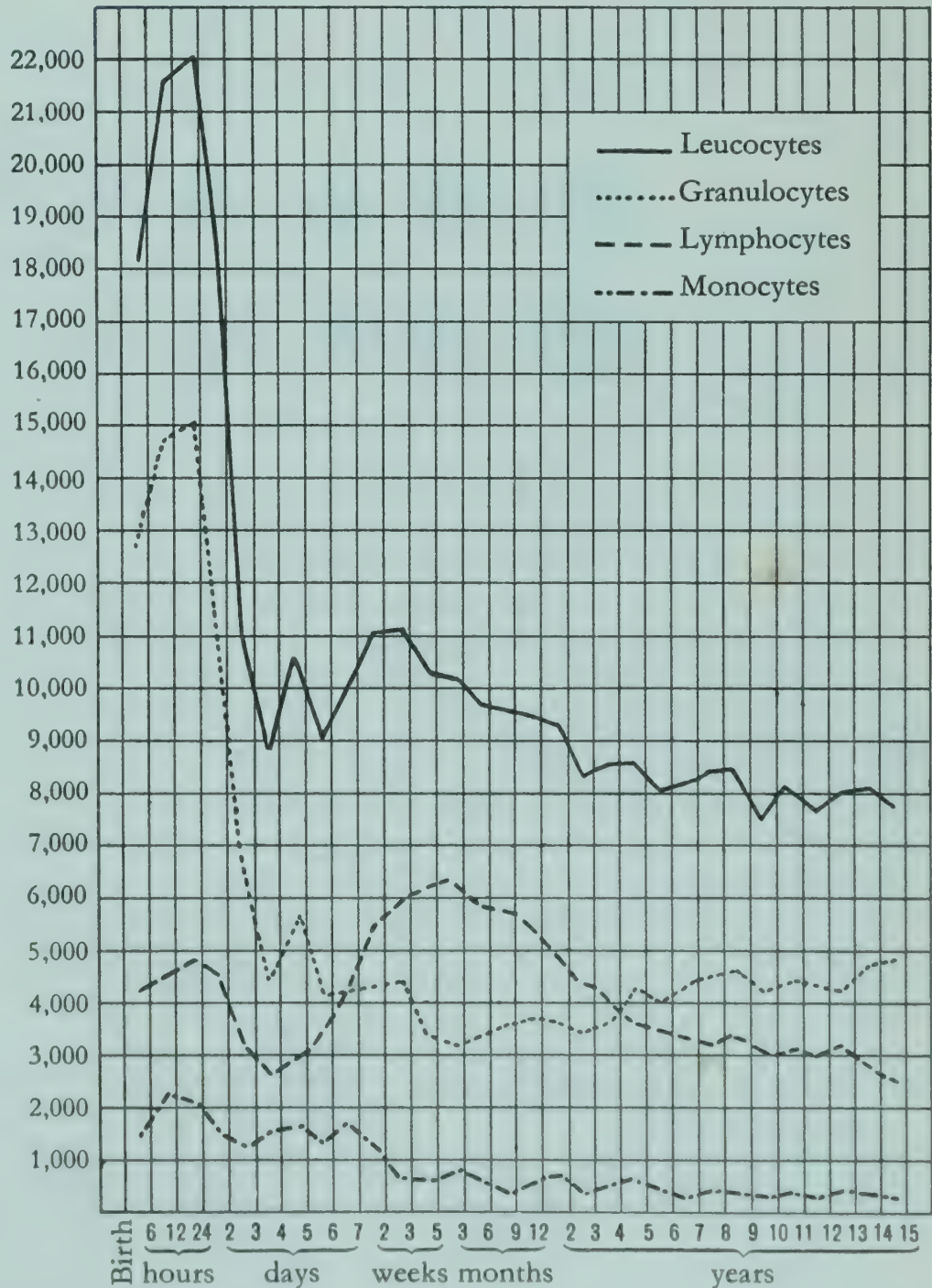
In fasting there is a significant fluctuation during the course of the day, inasmuch as ca. 23% of individuals show a fall in eosinophils during the day of 40% (highest eosinophil count in the morning). When not fasting, on the other hand, there is no significant fluctuation during the course of the day:

Non-fasting :

8 a.m. mean 180.5
11 a.m. mean 146.4
3 p.m. mean 150.2

Fall in leucocyte count between birth and 15 years

After KATO, K., *J. Pediat.*, 7, 7, 1935



1) After FORKNER, C. E., *Bull. Johns Hopk. Hosp.*, 45, 75, 1929.

2) After KOLMER, SPAULDING and ROBINSON, *Approved Laboratory Technic*, 5th ed., London, 1952.

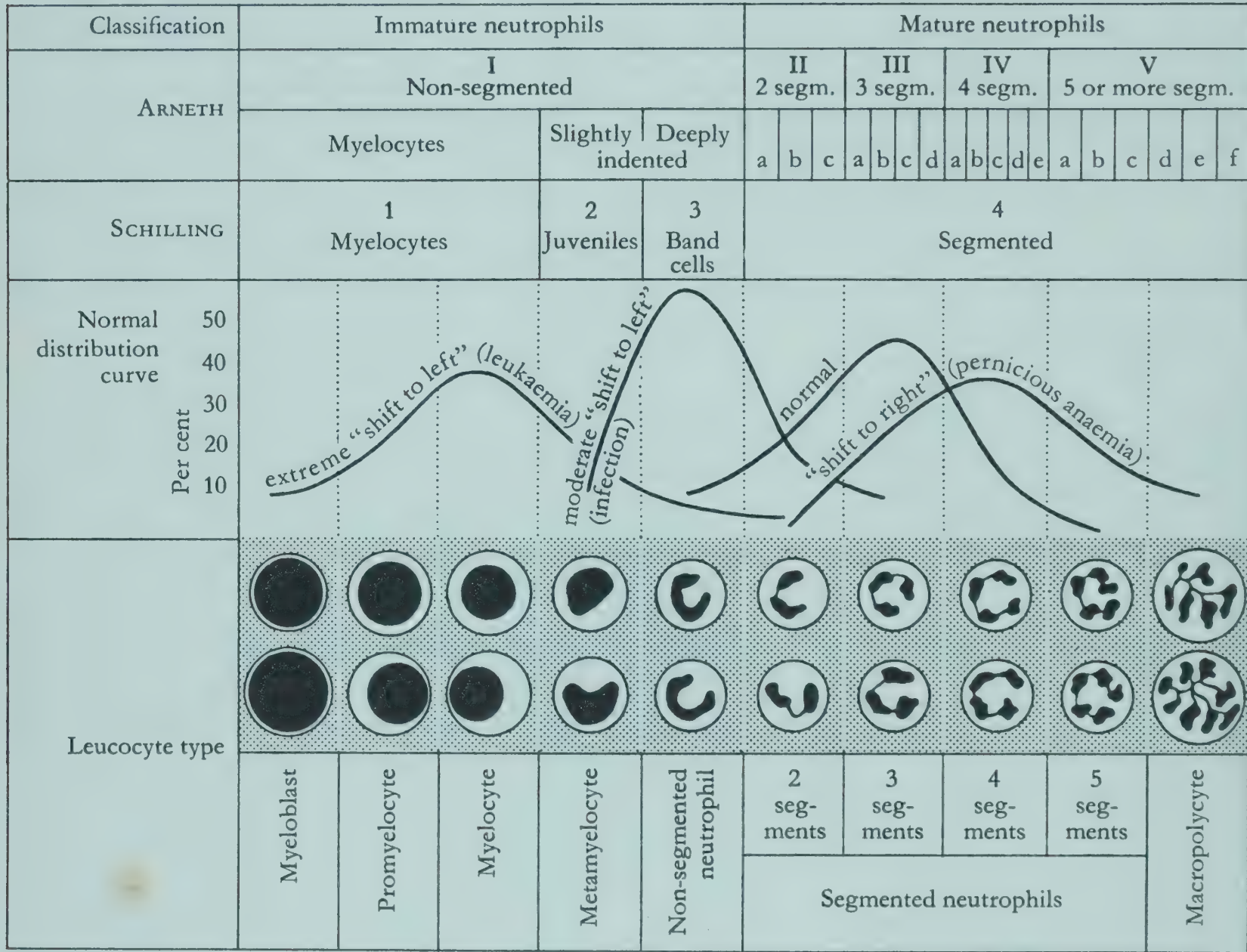
3) After KOLMER and BOERNER, *Approved Laboratory Technic*, 4th ed., New York, 1945.

4) After FISHER and FISHER, *Amer. J. med. Sci.*, 221, 121, 1951 (463 observations on 170 persons).

SCHILLING's haemogram

Normal ratio of immature neutrophils (myelocytes + juveniles + band cells) to mature (segmented) neutrophils = 1:13 or more	Basophils	Eosinophils	Myelocytes	Neutrophils			Lymphocytes	Monocytes
				juveniles	band cells	segmented cells		
Normal range (%)	0–1	2–4	0	0–1	3–5	51–67	21–35	4–8

Classifications of ARNETH and SCHILLING



Modified from HADEN, R. L., *Principles of Hematology*, 2nd ed., Philadelphia, 1940.

Bone marrow (cf. also genealogy of the blood corpuscles, page 332)

Myelogram (sternal marrow)¹: men and women as one group

Cell types			Mean ² %	Normal range ³ %
Red series 19.1%	Early erythroblasts 2.9%	Proerythroblasts	0.5	0.2 – 4.0
		Early normoblasts	2.4	1.5 – 5.8
	Late erythroblasts 16.2%	Intermediate normoblasts	11.7	5.0 –26.4
		Late normoblasts	4.5	1.6 –21.5
White series and others 70%	Granulocytes 57.4%	Myeloblasts	1.2	0.3 – 3.1
		Progranulocytes	3.0	0.5 – 4.5
		Myelocytes	8.7	0.9 –20.3
		Metamyelocytes	11.0	5.6 –22
		Band cells	17.9	6.1 –36
		Segmented cells	15.6	8.7 –27
	Others 12.6%	Lymphocytes	9.8	2.7 –24
		Monocytes	1.4	0.7 – 2.8
		Megakaryocytes	0.2	0.03– 0.4
		Plasmacytes	0.6	0.1 – 1.5
Reticulum cells		0.6	0.03– 1.6	
Not identifiable 10.9%		Unclassified cells	1.7	0.02– 3.3
		Disintegrated cells	9.2	1.1 –20.8

¹) From 21 authors (750 individuals), in ALBRITTON, E. C., *Standard Values in Blood*, Philadelphia, 1952.
²) Mean of authors' means. ³) Range of authors' means.

General

The division of human blood into the blood groups is a result of the isoantigenic² properties of the erythrocytes, properties which are inherited in accordance with Mendelian laws. The blood group to which an individual belongs thus depends absolutely on the blood groups of his ancestors and remains unchanged throughout his life.

The blood groups now recognized may be classified into systems according to their genotypic structure (see the following pages). *Inside* each of these systems there exists a precise relationship between the genes (or their allelomorphs) which determine the blood groups, whereas no such relationship exists *between* the various systems. The latter are accordingly inherited independently of one another. Up to the present 10 blood group systems have been discovered, not counting the secretor/non-secretor system.

Antibodies

The reaction antigen \longleftrightarrow antibody which distinguishes the blood groups belongs to the class of immune reactions. In principle there is no difference in this respect between the blood-group systems, in all of which sensitization, for example, is possible. There are, however, differences in the origins of the immunity and in the intensity of the immunization reactions.

In the ABO system, and very probably also in the system Jay, the antibodies are preformed (they appear shortly after birth and decrease with advancing age). See the diagram on the following page.

In the Rh system the antibodies are not preformed but appear only after the first immunization (transfusion with Rh-incompatible blood, Rh-incompatible pregnancy). After an immunization the titre of antibodies usually gradually returns to zero, leaving a sensitization which is often extremely high (in re-immunization titres as low as 1:10⁵ have been observed).

In the MN, P, Lutheran, Kell, Lewis and Duffy systems the antibodies are not at all or only occasionally preformed. Owing to the scarcity of statistical material it is not yet possible to decide

whether this is the result of a process of iso-immunization. The antigenicity of these systems is weak and although sensitization has already been observed it is so rare that it need only be taken into account in long series of transfusions.

The antibodies are classified in accordance with their capacity to agglutinate erythrocytes in suspension in various solutions, as follows:

Agglutinins: agglutinate erythrocytes in isotonic NaCl solution as well as in serum, in albumin solutions³ and in the so-called anti-human globulin solutions⁴.

Blocking antibodies: *do not* agglutinate erythrocytes in NaCl solutions but do so in serum, in albumin solutions and in anti-human globulin solutions.

Crytagglutinoids: agglutinate erythrocytes only in anti-human globulin solutions⁵.

The antibodies of the ABO system belong to the class of agglutinins. In about 30% of cases they are accompanied by corresponding isolsins, the nature of which is not yet known. In the Rh system all three antibodies can occur either singly or collectively; it is not clear whether this is a case of differing forms of one and the same substance.

All these antibodies are gamma-globulins (see page 313) and their presence in breast milk (colostrum) as well as in serum can be demonstrated. The blood-group substances or antigens (agglutinogens) are all glycoproteins with the exception of Rh antigen, which is a lipoprotein related to lecithin. The antigens of the ABO system are also secreted in saliva, breast milk, gastric juice, semen, etc. by a certain proportion of persons belonging to these blood groups, and their presence in these fluids can be demonstrated. Members of these blood groups may thus be divided into *secretors* and *non-secretors*, a circumstance of importance in forensic medicine (suspected rape; disputed paternity). For medico-legal aspects of the blood groups see footnote ⁶.

¹) Reviews: RACE and SANGER, *Bloodgroups in Man*, 2nd edition, Oxford, 1954; DAHR and REGENBOGEN, *Blutgruppenbestimmung und Bluttransfusion*, 2nd edition, Stuttgart, 1952; HOLLÄNDER, L., *Acta haemat.*, **6**, 377, 1951; ROSENFELD and VOGEL, *J. Mt Sinai Hosp.*, **20**, 89, 1953.

²) Iso- means "of the same species", hetero- "of a different species". Thus the Rh factor, or rather the Rh group D-d, was discovered through the immunization of rabbit heteroagglutinins by the blood of rhesus monkeys. The heteroagglutinins can be divided broadly into two categories: those which in animals are preformed, and those which appear after artificial immunization. The MN and P systems are characterized by heteroagglutinins since iso-agglutinins are extremely rare.

³) DIAMOND and DENTON, *J. Lab. clin. Med.*, **30**, 204, 1945.

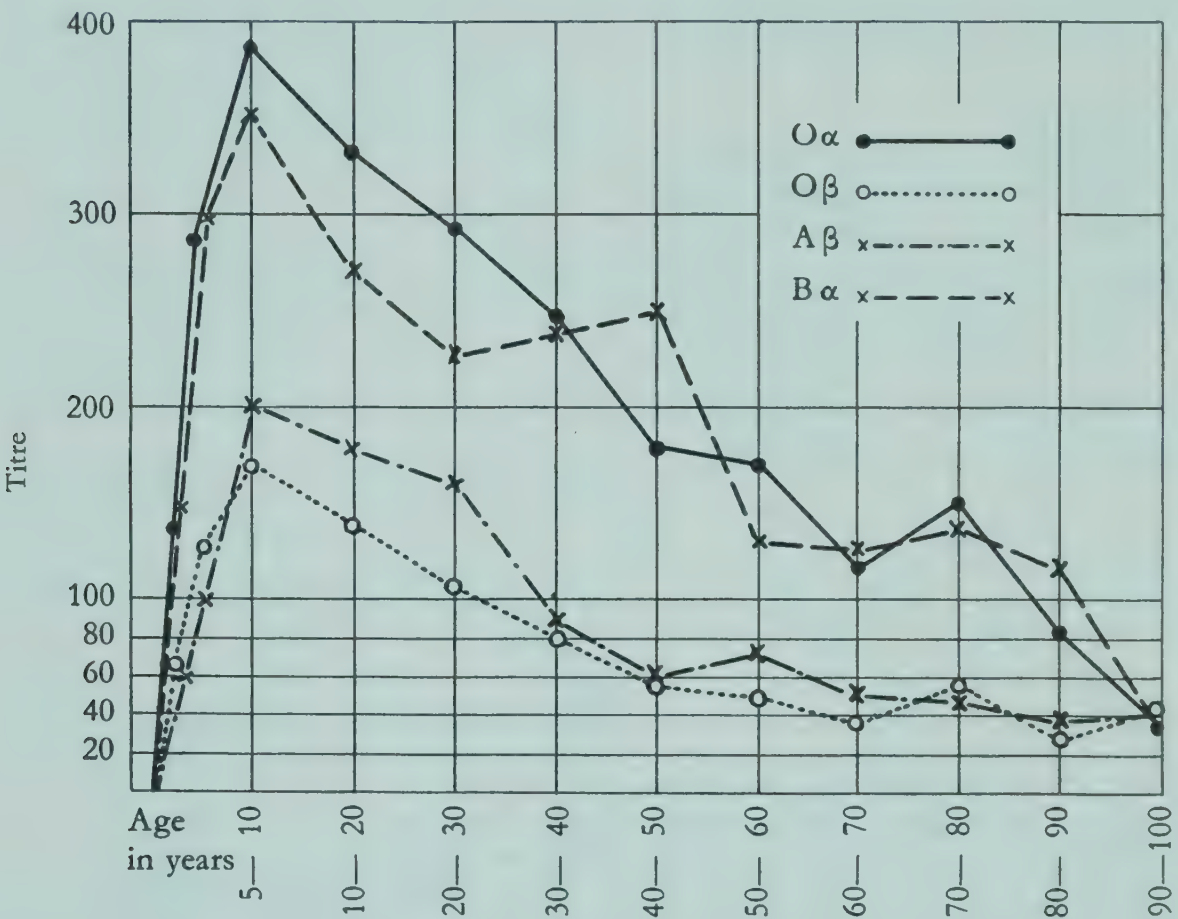
⁴) "Anti-human globulin solution" is the solution used in the COOMBS test (see under Blood transfusion, 1 (c), page 343). It is obtained by immunizing rabbits with human erythrocytes. The serum from the treated rabbits is neutralized by absorption of the antibodies on human erythrocytes.

⁵) HILL et al., *Blood*, Special Issue No. 2, 80, 1948.

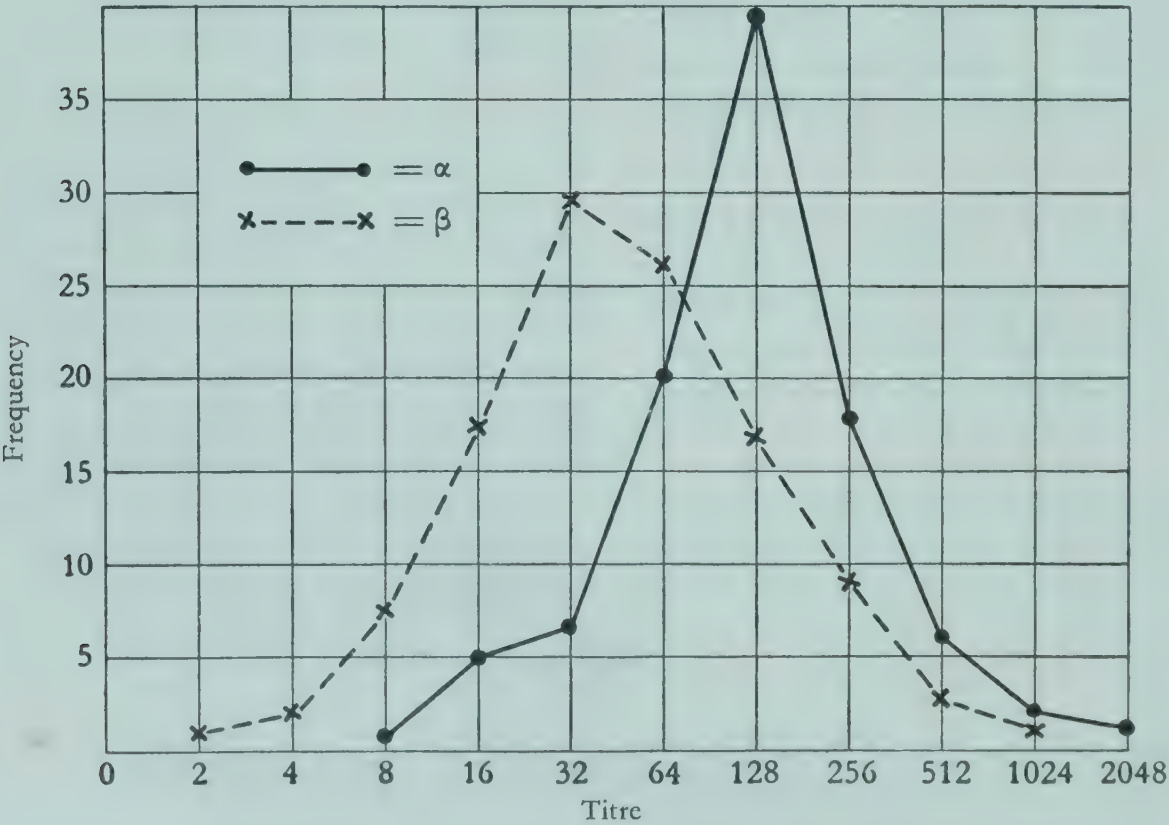
⁶) *Lancet* (Editorial), **1**, 296, 1952; *J. Amer. med. Ass.* (Editorial), **149**, 666, 1952.

The destructive action of the antibodies on erythrocytes *in vivo* is not identical with their *in vitro* effects mentioned on the previous page¹. In all cases *in vivo* the final result of the action of an antibody is the haemolysis of the antigenic erythrocytes. It is highly

probable that no agglutination takes place in the body², except in the case of a rapid and massive transfusion of incompatible blood. On the other hand the genotypic structure of the antigens appears to have an influence on the extent of haemolysis³.



Titre of ABO isoagglutinins throughout life. After THOMSEN and KETTEL, *Z. ImmunForsch.*, 63, 67, 1929.



Variation of the titre of α- and β-agglutinins in normal adults. After THOMSEN and KETTEL, *loc. cit.*

1) Since agglutinins, blocking antibodies and cryptagglutinoids, in spite of their differing agglutinating properties, all damage erythrocytes to the same extent, and since their respective titres appear to be unrelated, the precise extent of the immunization can only be obtained by measuring all three titres.

2) In erythroblastic infants born alive, absence of agglutination is often observed in spite of the presence of an antibody titre which *in vitro* would have more than sufficed, of the favourable conditions (serum as medium) and of the much longer time of exposure. WIENER, A. S., *Amer. J. clin. Path.*, 16, 477, 1946, attributed the kernicterus to thrombi in the liver arterioles; the observed thrombi were, however, later found to be postmortem changes.

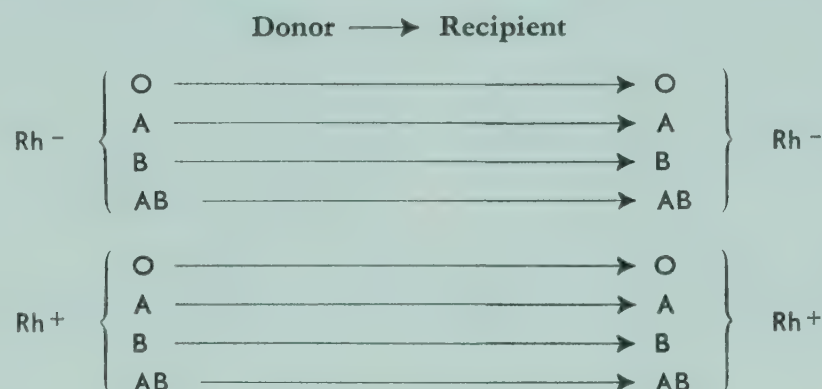
3) HILL and HABERMANN (see footnote ⁶ on previous page) observed that cryptagglutinoids had a ca. 100% greater haemolytic effect on homozygotic antigenic erythrocytes in the absence of complement than on heterozygotic erythrocytes,

Blood transfusion

The minimum conditions dictated by the mechanism of the blood group reactions, and by their relative frequency, antigenicity and tendency to sensitization, are as follows:

1. On principle only blood of the same group should be used:

(So-called “universal” donors—blood group O—should not be used indiscriminately: from the serological viewpoint such donors do not exist¹.)



If no blood compatible with the above scheme is available, emergency transfusions should be made as follows:



- (a) When Rh testing is impossible, women should receive ABO-compatible Rh-minus blood.
- (b) When a patient is to receive a *series of transfusions*, tests for the P, M, N and C, c factors should be made. If, as is usual, this cannot be done, the possibility of a reaction due to iso-immunization taking place should be avoided by crossmatching before each transfusion, *even when the same donor is used throughout* and preferably with erythrocytes suspended in serum or in albumin solutions.
- (c) *Previous transfusion*: Great care should be taken to ensure compatibility between donor and recipient when either has in the past received a transfusion, as also in the case of female recipients who are or have been pregnant. If in the latter case Rh testing for all the Rh factors Dd, Cc (possibly also Ee) is not possible, then compatibility should be tested by means of the COOMBS test² (but note that this test can only check compatibility with regard to the antibodies present, *it gives no indication that donor and recipient belong to the same Rh group*, and a possible sensitization cannot thereby be excluded); see also (a) above.
2. **Cross-matching**: To one drop of the recipient's serum on a slide or in a tube add one drop of the donor's blood corpuscles suspended in 20% bovine albumin solution, AB serum or the donor's own serum. If a slide is used it should be placed in a moist atmosphere (PETRI dish containing moistened filter paper) and observations made after standing for 15–30 minutes at 37°C. Tubes are best read after centrifuging for ½ minute at 2000 r.p.m. The same applies to operations at room temperature. The donor serum can of course be checked in the same way against the recipient's corpuscles (complete cross-matching). Cross-matching performed in this way reveals incompatibilities in all blood groups, with the possible exception of the Duffy system, since Duffy antibodies generally react only under the indirect anti-globulin method (COOMBS test). The latter test is therefore recommended in all cases where a patient is to be given many transfusions.
3. **OEHLCKER's biological test**: Before commencing the transfusion ca. 20 ml of the donor's blood is injected i.v. rapidly and with considerable pressure. If in 3 minutes the recipient shows no signs of incompatibility (discomfort, collapse, backache, etc.) the transfusion may be proceeded with. This test cannot be made on anaesthetized patients. It should be avoided as far as possible, since the injected blood can lead to Rh-sensitization or in the case of patients already Rh-sensitized, to an immune reaction appearing only after several hours.
4. In **emergency**: If testing is impossible, or if the blood groups of donor and recipient are unknown, or if a known supply of blood is not available, *cross-matching at room temperature*, for example by the following method, should be undertaken:
- A drop of the recipient's blood is mixed with chloroform and smeared on to a slide (chloroform has a haemolytic action). After evaporation of the chloroform a haemoglobin-containing plasma is left which with advantage is now diluted with a drop of isotonic sodium citrate solution. To the drop of recipient's blood so prepared one drop of the donor blood is now added. If no agglutination occurs after several minutes it can be assumed that the donor blood is suitable³.
- As an extra precaution (particularly when large quantities are to be transfused) a simultaneous test *vice versa* is recommended. Since the erythrocytes of the one party are excluded this method gives a clear answer to the question “who agglutinates whom?”

¹) WILLENEGGER, H., *Bull. Schweiz. Akad. med. Wiss.*, **8**, 285, 1952.

²) COOMBS et al., *Brit. J. exp. Path.*, **26**, 255, 1945; *Lancet*, **1**, 264, 1946.

³) CLEMENS, *Med. Mscr.*, **3**, 195, 1949.

Blood group system ABO

The groups A, B, O were discovered by LANDSTEINER¹; the subgroups A₁ and A₂ were described by VON DUNGERN and HIRSZFELD² as reacting with anti-A sera in a quantitatively different manner; LANDSTEINER, WITT and LEVINE^{3, 4} showed, however, that the difference is qualitative. BERNSTEIN⁵ was the first to present the 3-gene (3-allelomorph) theory, from which THOMSEN, FRIEDENREICH and WORSAAE⁶ developed the 4-gene (4-allelomorph) theory which embraces also the subgroups A₁ and A₂ (see the schemes below). Further A subgroups A₃, A₄, A₅ have since been discovered, but these are extremely rare.

The structure of the ABO system has been still further complicated by the discovery of a new factor H^{12, 13}. It has been suggested that the factors A, B, O are mutants of this H factor¹², a conception which sets in a new light the theory of incomplete mutation, the pleiades, and of the genesis of transitional forms between O and A₂ (A₅, A₄, A₃)¹⁵ postulated by HIRSZFELD and AMZEL¹⁴. Clinically, the H factor may be ignored.

Scheme of the 4-gene theory: A ₁ , A ₂ , B, O							Scheme of the 3-gene theory: A, B, O					
Genes	Relative frequency ⁷ %	Genotypes	Relative frequency ⁸ %	Phenotypes	Relative frequency ⁹ %	Antibodies (agglutinins) (serum)	Genes	Relative frequency ^{7, 10} %	Genotypes	Phenotypes	Relative frequency ⁹ %	Antibodies (agglutinins) (serum)
A ₁	25.93	A ₁ A ₁ A ₁ A ₂ A ₁ O	4.2 30.2	A ₁	34.4	{ Anti-B and very rarely Anti-A ₂	A	31.612	AA AO	A	46.8 ¹¹	Anti-B (β)
A ₂	6.49	A ₂ A ₂ A ₂ O	12.4	A ₂	12.4	{ Anti-B and sometimes Anti-A ₁						
		A ₁ B	2.4	A ₁ B	2.4	{ very rarely Anti-A ₂ , no Anti-B			AB	AB	4.0	{ see the column Antibodies in the 4-gene scheme on the left
		A ₂ B	1.6	A ₂ B	1.6	{ often Anti-A ₁ , no Anti-B						
B	5.99	BB BO	0.0 6.4	B	6.4	{ Anti-A ₁ + Anti-A ₂	B	6.228	BB BO	B	6.4 ¹¹	Anti-A (α)
O	61.59	OO	42.8	O	42.8	{ Anti-A ₁ + Anti-A ₂ + Anti-B	O	62.160	OO	O	42.8	{ Anti-A (α) + Anti-B (β)

Inheritance: A₁ is dominant over A₂. A₁ and A₂ (= A in the simplified scheme) are “combinant” (neither dominant nor recessive) with regard to B. A₁ and A₂ (= A) and B are dominant over O. O is recessive and appears therefore as phenotype only in homozygotes.

¹) LANDSTEINER, K., *Zbl. Bakt.*, **27**, 357, 1900; *Wien. klin. Wschr.*, **14**, 1132, 1901.
²) VON DUNGERN and HIRSZFELD, *Z. Immunforsch.*, **8**, 526, 1911.
³) LANDSTEINER and WITT, *J. Immunol.*, **11**, 221, 1926.
⁴) LANDSTEINER and LEVINE, *ibid.*, **12**, 441, 1926.
⁵) BERNSTEIN, F., *Klin. Wschr.*, **3**, 1495, 1924.
⁶) THOMSEN et al., *Hospitalstidende*, **72**, 1077, 1929; *Klin. Wschr.*, **9**, 67, 1930.
⁷) HARTMANN and LUNDEVALL, *Blood Group Distribution in Norway, with Special Regard to the MN and O A₁ A₂ B System*, Oslo, 1944.
⁸) BOORMAN et al., *Ann. Eugen.*, **14**, 201, 1948.
⁹) Calculated from ⁸.
¹⁰) HARTMANN et al., *Blood Group Distribution in Norway*, Oslo, 1941.
¹¹) Group A is the most widely distributed in Europe, group B in Asia (after HIRSZFELD and HIRSZFELD, *Lancet*, **1**, 675, 1919).
¹²) MORGAN and WATKINS, *Brit. J. exp. Path.*, **29**, 159, 1948; BOORMAN et al., *Ann. Eugen.*, **14**, 201, 1948.
¹³) BHENDE et al., *Lancet*, **1**, 903, 1952.
¹⁴) HIRSZFELD and AMZEL, *Ann. Inst. Pasteur*, **65**, 251, 1940.
¹⁵) HOLLÄNDER, L., *Acta haemat.*, **6**, 377, 1951.

Blood group system MNSs

The blood group system MN was discovered by LANDSTEINER and LEVINE^{1,2} in 1927 using rabbit heteroagglutinins; the hereditary theory of the same authors³ has been confirmed by SCHIFF⁴ and by WIENER⁵.

In 1947 came the discovery of a further antigen which is inherited together with the antigens M, N (WALSH and MONTGOMERY⁶, SANGER and RACE⁷) and which led to the further subdivision (linked genes) of this blood group system. The new gene was denoted by S and its allelomorph by s¹⁷ (these symbols should not be confused with those earlier used for secretor, S, and non-secretor, s). The antigen S was discovered through the antibody (agglutinin) anti-S of a patient who had received several transfusions. Anti-S heteroagglutinins of other species have not yet been found, nor has it been found possible to stimulate their formation. The first anti-s antibody was discovered in the serum of the mother of an infant suffering from haemolytic disease¹⁷, the

second in the serum of a volunteer who had been purposely immunized¹⁸.

The antibodies (agglutinins) of the MNSs system are quite often preformed but usually inactive at body temperature (cold agglutinins). In practice they are therefore of little clinical importance, except possibly in long series of transfusions. Many cases of haemolytic disease of the newborn due to anti-S have already been observed. The MNSs system is mainly of importance in forensic medicine, and in human genetic and ethnological studies⁸, where it is of considerably greater significance than the other blood group systems.

Inheritance: M and N are "combinant", i.e. the phenotype MN possesses both the genes M and N. S and s are likewise inherited in combination. The genes M and N are coupled with the genes S and s since they are carried by the same chromosome.

Schematic representation of the blood group system MNSs

MN scheme						Ss scheme					Complete scheme of the MNSs system						
Genes	Relative frequency ⁸ %	Genotypes	Phenotypes	Relative frequency ⁸ %	Possible antibodies (serum)	Genes	Relative frequency ⁸ %	Genotypes	Phenotypes	Relative frequency ⁸ %	Comb. genes	Relative frequency ⁸ %	Genotypes	Relative frequency ⁸ %	Phenotypes	Relative frequency ⁸ %	Possible antibodies (serum)
M	53.165	MM	M	28.38	Anti-N	S	32.73802	SS	S	10.7177	MS Ms	24.71722 28.31308	MSMS MSMs Ms Ms	6.1094 13.9964 8.0163	MS Ms	20.1058 8.0163	Anti-N, Anti-s Anti-N, Anti-S
		MN	MN	49.57	none			Ss	S	44.0405		MSNS MSNs Ms NS Ms Ns	3.9650 19.2542 4.5419 22.0563	MNS MNs	27.7611 22.0563	Anti-s Anti-S	
N	46.835	NN	N	22.05	Anti-M	s	67.26198				NS Ns	8.02080 38.94890	NSNS NSNs Ns Ns	0.6433 6.2480 15.1702	NS Ns	6.8913 15.1702	Anti-M, Anti-s Anti-M, Anti-S

Blood group system Pp (P⁺, P⁻)

The blood group system Pp was discovered by LANDSTEINER and LEVINE² in 1927 using rabbit heteroagglutinins; the hereditary theory of the same authors^{9,10} has been confirmed principally by DAHR^{11,12}. The dominant gene is denoted by P (P⁺) and its recessive allelomorph, which has no antigenic properties, by p (P⁻); p thus denotes absence of P, whence the symbol P⁻.

The anti-P antibody (agglutinin) is very widely distributed both in man¹³ and animals. It is so weak, however, that this blood group system is only of importance when long series of transfusions are made. In this case, tests for this antibody are absolutely necessary since it has already been responsible for severe haemolytic reactions with fatal outcome¹⁴.

Schematic representation of the blood group system Pp

Genes	Frequency ¹⁵ %	Genotypes	Frequency ¹⁶ %	Phenotypes	Frequency ¹⁶ %	Antibodies (agglutinins) (in serum)
P	50.6	PP	25.6	P	75.5	No antibodies
		Pp	49.9			
p	49.4	pp	24.5	p	24.5	Anti-P

¹) LANDSTEINER and LEVINE, *Proc. Soc. exp. Biol.*, **24**, 600, 1927. ²) LANDSTEINER and LEVINE, *ibid.*, **24**, 941, 1927. ³) LANDSTEINER and LEVINE, *ibid.*, **25**, 672, 1928; *J. exp. Med.*, **48**, 731, 1928. ⁴) SCHIFF, F., *Klin. Wschr.*, **2**, 1956, 1930. WIENER and VAISBERG, *J. Immunol.*, **20**, 371, 1931. ⁵) WALSH and MONTGOMERY, *Nature (Lond.)*, **160**, 504, 1947. ⁶) SANGER and RACE, *ibid.*, **160**, 505, 1947. ⁷) Observed and calculated values from RACE and SANGER, *Blood Groups in Man*, 2nd edition, Oxford, 1954. ⁸) LANDSTEINER and LEVINE, *J. Immunol.*, **18**, 87, 1930. ⁹) LANDSTEINER and LEVINE, *ibid.*, **20**, 179, 1931. ¹⁰) DAHR, P., *Z. Immunforsch.*, **97**, 168, 1940. ¹¹) DAHR, P., *ibid.*, **101**, 346, 1942. ¹²) HENNINGSEN, K., *Acta path. microbiol. scand.*, **26**, 639, 1949. ¹³) MOUREAU, P., *Rev. belge Sci. méd.*, **16**, 258, 1945. ¹⁴) Means calculated from the values of 5 authors (9405 tests): DAHR, P., see ¹¹; HENNINGSEN, K., see ¹²; JONSSON, B., quoted by HENNINGSEN ¹³; JUNGMICHEL, G., *Z. geront. Med.*, **36**, 259, 1942; SANGER et al., *Rev. Hémat.*, **4**, 28, 1949. ¹⁵) Calculated from ¹⁶. ¹⁷) LEVINE et al., *Proc. Soc. exp. Biol.*, **78**, 218, 1951. ¹⁸) SANGER et al., *Vox sanguinis*, **3**, 71, 1953.

Blood group system Rh¹

The blood group system Rh, or rather one of its antigens, D (see later in this section), was discovered by LANDSTEINER and WIENER² using heteroagglutinins from rabbits and guinea pigs which had been immunized with the blood of rhesus monkeys (*Macacus rhesus*). Genetical theories have been put forward by WIENER³ (6 combinant allelomorphs), by RACE⁴ (7 combinant allelomorphs) and finally by FISHER⁵ (3 linked allelomorph pairs on the same chromosome). Since FISHER's theory is the only one which provides an explanation of all the relations in the Rh system (particularly the structure of the genotypes) his nomenclature will be used exclusively in this section. For purposes of comparison the nomenclatures of WIENER and of RACE are also given in the table on page 349.



From the relative frequency of the Rh combinations it can be calculated that the distance between the positions D-d and C-c must be greater than that between C-c and E-e^{5,11,12}.

Genotypes and phenotypes

All 6 allelomorphs form an antigen appearing phenotypically in the erythrocytes. Each individual thus possesses a combination of 6 Rh antigens. In the Rh group the phenotypes and genotypes therefore correspond*. Altogether 36 genotypes or phenotypes are possible (disregarding C^w, D^u, F and f). Cf. the table on page 348.

Structure

The Rh blood group system is due to the existence of three allelomorph pairs linked to the one chromosome at three different points. FISHER's notation for these three pairs is: D-d, C-c, E-e. Further allelomorphs C^w (^{6,7}), D^u (⁸), E^u (⁹), c^w (¹⁰) have also been found, as well as a fourth allelomorph pair F, f (RACE²⁴). The latter is of little clinical importance but of great theoretical interest. In the interests of simplification it will be disregarded here. The disposition of the Rh genes on the chromosome may be represented as follows^{5,11,12}:

Any person who is homozygous with respect to one antigen can be immunized by the corresponding allelomorph (antigen) as a result of an incompatible blood transfusion or incompatible pregnancy. If, for example, a phenotype cde/cde is transfused with blood of the gene structure CDe/cDE, the antibodies anti-D and possibly also anti-C and anti-E will be formed in the serum. The Rh factors have differing antigenic activities:

D > E > C > c > e > d

as shown by the following table:

Relative frequency of the antibodies found in Rh-sensitized persons¹

Antibodies		Sera containing these antibodies usually belong to the following genotypes	Relative frequency %
agglutinating erythrocytes in physiological salt solutions (agglutinins)	agglutinating erythrocytes in albumin solutions (blocking antibodies)		
Anti-D Anti-D —	Anti-D — Anti-D	} cde/cde (or Cde/cde or cdE/cde)	60 or more
Anti-D + anti-C Anti-D + anti-C	Anti-D —		
Anti-D + anti-E Anti-D + anti-E	Anti-D —	} cde/cde (or Cde/cde)	2
Anti-C	Anti-D		
Anti-E	Anti-D	cde/cde	1
Anti-E	—	CDe/CDe (or CDe/cde)	1
Anti-c —	— Anti-c	} CDe/CDe (or CDe/cde)	1
Anti-e	Anti-e		
Anti-C	Anti-C	cDE/cDE and cDE/cde	rare
Anti-d	Anti-d	CDe/CDe	rare

Each of these antibodies exerts, independently of the others, an agglutinating, blocking and haemolyzing effect on incompatible erythrocytes (see page 341). It is always the allelomorphic antigen

which is incompatible; thus the antigen c produces the antibody anti-C when stimulated by C erythrocytes.

* Since the antigenicity of the factors D, C and E greatly exceeds that of d, c and e, the former were originally thought to be the dominant allelomorphs (hence their notation with capital letters). Now that all the antibodies have been found, however, the distinction between dominant and recessive is no longer correct. The distinction between phenotypes and genotypes can likewise no longer be made.

Since the Rh antibodies are formed and act independently of each other, in spite of the fact that the antigens producing them are linked to the same chromosome, the Rh system may be divided for the sake of simplification into 3 subgroups: C–c, D–d and E–e. Clinically these subgroups may simply be regarded as special blood groups additional to those existing apart from the Rh system.

Scheme of the 3 Rh subgroups. (The frequencies given are those found for the English population but are valid within a few per cent for all white races.)

The Rh chromosome consists of the following 3-group system	with the following	Genes		which combine to give the following possible	Genotypes		with the following antibodies	
		allelo-morphs	% frequency ¹²		geno-types	% frequency ¹³	the participation of which in the total recorded cases of erythroblastosis foetalis amounts to:	
D–d		d	41.03		dd	16.8 Anti-D 92%
		D	58.97		Dd	48.4 Anti-d	} 8%
					DD	34.8 Anti-C	
C–c		c	56.73		cc	32.2 Anti-c	
		C	43.27		Cc	49.1 Anti-E	
					CC	18.7 Anti-e	
E–e		e	84.46		ee	71.3		
		E	15.54		Ee	26.3		
					EE	2.4		

As this scheme shows, the antibody anti-D is by far the commonest. This is due to the high antigenicity of the subgroup D–d in comparison with the other subgroups, and in fact the discovery of the Rh system (LANDSTEINER and WIENER²) was due to the activity of this subgroup. The whole Rh system may indeed be justifiably divided into two classes, Rh⁺ and Rh[–], in accordance with the occurrence of the Rh-subgroup genes D and d. The Rh⁺ class consists of the genotypes DD and Dd and the Rh[–] class of the genotypes dd. Routine blood-group determinations prior to transfusions, particularly in the case of women and girls, should include this simplified Rh classification Rh⁺ or Rh[–].

Relative frequencies of the Rh⁺ and Rh[–] classes

	Number of persons tested	Relative frequency (%)	
		Rh ⁺	Rh [–]
America (whites) ¹⁴	23,403	85.77	14.23
Belgium ¹⁷	113	80.53	19.47
England ¹⁴	10,231	84.09	15.91
France ¹⁶	1190	85.88	14.12
Norway ¹⁰	24,051	84.56	15.44
Sweden ¹⁵	937	86.55	13.45
Switzerland ¹⁸	1522	84.17	15.83

The highest Rh[–] frequency so far recorded was found among the inhabitants of the Vals valley, Canton Grisons, Switzerland (30–48.4% according to locality)²³.

Determination of genotypes

Apart from their use in forensic medicine, the Rh genotypes are of prognostic importance in cases of incompatible pregnancy with respect to future pregnancies.

The complete phenotype or genotype can often be deduced directly, according to the antisera available for testing. If, for example, erythrocytes are tested with the antisera now available, anti-D, anti-C, anti-E, anti-c and anti-e, and no agglutination results from the first three of these, then the “empirical formula” for these erythrocytes is ccddee, from which follows the genotype cde/cde since for each allelomorph only two chromosomes are available. As an example, in order to find out whether a Rh⁺ person is homozygous or heterozygous a test is made with the antiserum anti-D; since this gene appears to be dominant the genotype can be either DD or Dd. A further test with anti-d must therefore be made; if this test is negative then the person is DD, if positive he is Dd. The antisera anti-d, anti-c and anti-e are relatively rare, however, particularly the important anti-d which has up to now been found in only two cases. A genotype with incompletely determined gene structure must therefore be assessed on the basis of observed genotype frequencies, a method which naturally can never be exact. For this purpose the table on page 349 is used. Example: the incomplete gene structure cDE has been determined, for which there are the following five possible genotypes (see this table):

Possible genotypes	Frequency in the Rh system	Frequency with respect to the incomplete gene structure cDE
(1) cDE/cDE	1.9906 %	14.0 %
(2) cDE/cdE	0.3353 %	2.3 %
(3) cDE/cDe	0.7243 %	5.2 %
(4) cDE/cde	10.9657 %	78.0 %
(5) cDe/cdE	0.0610 %	0.5 %
Total	14.0769 %	100 %

It follows that this sample with incompletely determined gene structure cDE belongs with 78% probability to the genotype cDE/cde. A more exact result would be obtained by further testing with anti-c and anti-e sera (for the above example only the latter serum would be required).

The total number of possible genotypes is 36, as illustrated by the following scheme:

CDe/CDe	cde/cde	cDE/cDE	cDe/cDe	cdE/cdE	Cde/Cde	CDE/CDE	CdE/CdE
CDe/cde	←	←	←	←	←	←	←
CDe/cDE	cde/cDE	←	←	←	←	←	←
CDe/cDe	cde/cDe	cDE/cDe	←	←	←	←	←
CDe/cdE	cde/cdE	cDE/cdE	cDe/cdE	←	←	←	←
CDe/Cde	cde/Cde	cDE/Cde	cDe/Cde	cdE/Cde	←	←	←
CDe/CDE	cde/CDE	cDE/CDE	cDe/CDE	cdE/CDE	Cde/CDE	←	←
CDe/CdE	cde/CdE	cDE/CdE	cDe/CdE	cdE/CdE	Cde/CdE	CDE/CdE	←

The frequency distribution for these genotypes is given in the summary on the opposite page.

Clinical significance

(The following remarks apply only to the Rh subgroup D-d: Rh+ = phenotype D [genotype DD or Dd]; Rh- = phenotype d [genotype dd].)

Rh antibodies are found only in a small proportion of Rh-negative persons: in some Rh-negative women who have had a number of Rh-positive children, and in Rh-negative persons of both sexes who in the past have received several Rh-incompatible blood transfusions or injections. Apart from these special cases the blood of Rh-negative persons is free of Rh antibodies, which explains why the transfusion of Rh+ blood into Rh-negative persons usually provokes no reaction. Nevertheless the determination of the Rh type prior to blood transfusions is today an absolute necessity, particularly in women and girls of child-bearing age, in women who have already given birth and in persons of both sexes who either have a history of blood transfusion or who must receive a long series of transfusions. In the former cases it is a question of preventing a sensitization and its tragic consequences for the offspring, in the latter cases of avoiding a possible immunization which can be of any degree of severity according to the circumstances of the case.

Not all Rh-negative persons react equally strongly to immunization (by incompatible blood or incompatible pregnancy). As a rule immunization occurs only after a number of transfusions of incompatible blood and is most severe when the transfusions are given at intervals of several months. Here the amount of blood transfused is of no consequence, even 0.5 ml can have a maximal immunizing effect. Incompatible pregnancies have a similar effect. The first child (provided that the mother has not already been sensitized by a transfusion) is usually unaffected (exceptions are known), the danger is greatly increased in the second pregnancy while the outlook for the third is very poor.

Once immunization has occurred it is followed by lifelong

sensitization, often at an extremely high level, even when the titre of antibodies has again fallen to zero. The effect of this sensitization is such a further incompatible blood transfusion or pregnancy is followed by the very rapid formation of antibodies in extremely large amounts, often resulting in a severe reaction. How serious the consequences can be is illustrated by the recorded case²⁰ of a Rh-negative woman who had been sensitized at the age of 7 years by a blood transfusion. Her first child, born 16 years after the transfusion, died of severe prenatal injury 6 hours after delivery.

If a woman has once been delivered of an erythroblastic child the prognosis for later pregnancies, if the father is homozygous, is unquestionably bad. If the father is heterozygous there is a chance that 50% of the offspring will be healthy. The only way at present known by which the life of a Rh-affected child may be saved is by an exchange transfusion immediately after delivery. Since it is not always possible at the moment of birth to make a definite assessment of injury, this procedure should in any case be adopted when it is known that the mother has already given birth to seriously affected children. Even with a nearly normal blood picture, normal haemoglobin content and absence of icteric symptoms a severe jaundice can develop within several hours after birth. An exchange transfusion is then often too late, i.e. even if it saves the life of the child there remains the considerable danger of permanent injury due to kernicterus. In serious cases in which there is practically no hope of the child being born alive the sole possibility consists in premature delivery (ca. 1 month before term) by caesarean section followed by immediate exchange transfusion. This is, however, a last resort, since it has been shown that prematurely-born children are much more likely to contract kernicterus than full-term children²¹.

For the technique of blood exchange see inter alia WIENER and WEXLER²² and MOLLISON and WALKER²¹.

¹) MOLLISON, MOURANT and RACE, *The Rb Blood Groups and their Clinical Effects*, Medical Research Council Mem. 27, London, 1952. ²) LANDSTEINER and WIENER, *Proc. Soc. exp. Biol.*, 43, 223, 1940; *J. exp. Med.*, 74, 309, 1941. ³) WIENER, A.S., *Proc. Soc. exp. Biol.*, 54, 316, 1943. ⁴) RACE et al., *Nature (Lond.)*, 153, 52, 1944. ⁵) FISHER and RACE, *ibid.*, 157, 48, 1946. ⁶) CALLENDER and RACE, *Ann. Eugen.*, 13, 102, 1946. ⁷) RACE et al., *Heredity*, 2, 237, 1948. ⁸) STRATTON, F., *Nature (Lond.)*, 158, 25, 1946. ⁹) CEPPELINI, IKIN and MOURANT, *Boll. Ist. sieroter. milan.*, 29, 123, 1950; MOURANT et al., *Schweiz. med. Wschr.*, 82, 1100, 1952. ¹⁰) RACE, SANGER and LAWLER, *Nature (Lond.)*, 161, 316, 1948; *Heredity*, 2, 237, 1948; JONES, A., et al., *Science*, 118, 721, 1953. ¹¹) FISHER, R. A., *Amer. Sci.*, 35, 95, 1947. ¹²) RACE et al., *Blood*, 3, 689, 1948. ¹³) Calculated from ¹². ¹⁴) RACE and SANGER, *Blood Groups in Man*, 2nd edition, Oxford, 1954. ¹⁵) BROMAN, B., *Acta paediat.*, 31, Suppl. 2, 1944. ¹⁶) TZANK and BESSIS, *Communiqué de la Société d'Hématol.*, 20th Dec., 1945. ¹⁷) MOUREAU, P., *Acta biol. belg.*, 1, 123, 1941. ¹⁸) ZIEGLER, E., personal communication to RACE and SANGER¹⁴, 1949. ¹⁹) HARTMANN, O., personal communication to RACE and SANGER¹⁴, 1949. ²⁰) WILLI, H., unpublished, Zurich, 1948. ²¹) MOLLISON and WALKER, *Lancet*, 1, 429, 1952. ²²) WIENER and WEXLER, *Pediatrics*, 8, 117, 1951. ²³) MOOR-JANKOWSKI, J. K., *Schweiz. med. Wschr.*, 83, 1044, 1953. ²⁴) ROSENFELD et al., *Brit. med. J.*, 1, 975, 1953.

Rh genotypes in the English population
(after RACE et al., *Blood*, 3, 689, 1948)

Calculated group frequency (%) (if only first 4 sera used)	The 4 antisera fairly widely available				Rarer antisera				Genotype (FISHER's notation)	Short symbols		Calculated genotype frequency (%) (using all 8 sera)
	C+C ^w	c	D	E	pure C	pure C ^w	e	d		RACE	WIENER	
15.1020	—	+	—	—	—	—	+	+	cde/cde	rr	rr	15.1020
2.0609	—	+	+	—	{	{	+	+	cDe/cde cDe/cDe	R ₀ r R ₀ R ₀	R ⁰ r R ⁰ R ⁰	1.9950 0.0659
							+	—				
0.9376	—	+	—	+	{	{	+	+	cdE/cde cdE/cdE	R''r R''R''	r''r r''r''	0.9235 0.0141
							—	+				
14.0769	—	+	+	+	{	{	—	—	cDE/cDE cDE/cdE cDE/cDe cDE/cde cDe/cdE	R ₂ R ₂ R ₂ R'' R ₂ R ₀ R ₂ r R ₀ R''	R ² R ² R ² r'' R ² R ⁰ R ² r R ⁰ r''	1.9906 0.3353 0.7243 10.9657 0.0610
							—	—				
							—	+				
							+	—				
							+	+				
0.7644	+	+	—	—	{	{	+	+	Cde/cde C ^w de/cde	R'r R' ^w r	r'r r ^w r	0.7644 0.0000
							—	+				
34.8899	+	+	+	—	{	{	+	—	CDe/cDe CDe/cde cDe/Cde C ^w De/cDe C ^w De/cde C ^w de/cDe	R ₁ R ₀ R ₁ r R ₀ R' R ₁ ^w R ₀ R ₁ ^w r R' ^w R ₀	R ¹ R ⁰ R ¹ r R ⁰ R' R ^w R ⁰ R ^w r r ^w R ⁰	2.0922 31.6759 0.0505 0.0664 1.0049 0.0000
							+	+				
							—	+				
							+	—				
							+	+				
0.0234	+	+	—	+	{	{	+	+	cdE/Cde CdE/cde CdE/cdE C ^w de/cdE	R''R' R _y r R _y R'' R' ^w R''	r''r' r _y r r _y r'' r ^w r''	0.0234 0.0000 0.0000 0.0000
							+	—				
							—	+				
							+	+				
13.4178	+	+	+	+	{	{	+	—	CDe/cDE cDe/CDE CDe/cdE cDE/Cde CDE/cde CdE/cDe cDE/CDE cdE/CDE CdE/cDE C ^w De/cDE C ^w De/cdE C ^w de/cDE	R ₁ R ₂ R ₀ R ₂ R ₁ R'' R ₂ R' R ₂ r R _y R ₀ R ₂ R ₂ R''R ₂ R _y R ₂ R ₁ ^w R ₂ R ₁ ^w R'' R' ^w R ₂	R ¹ R ² R ⁰ R ₂ R ¹ r'' R ² r' R ₂ r r _y R ⁰ R ² R ₂ r''R ₂ r _y R ² R ^w R ² R ^w r'' r ^w R ²	11.5000 0.0125 0.9685 0.2775 0.1893 0.0000 0.0687 0.0058 0.0000 0.3648 0.0307 0.0000
							+	+				
							+	—				
							—	—				
							—	+				
							+	+				
							+	—				
							—	+				
							+	+				
							+	—				
							—	+				
							+	+				
							+	+				
							+	+				
0.0097	+	—	—	—	{	{	+	+	Cde/Cde C ^w de/Cde C ^w de/C ^w de	R'R' R' ^w R' R' ^w R' ^w	r'r' r ^w r' r ^w r ^w	0.0097 0.0000 0.0000
							+	+				
							—	+				
18.5073	+	—	+	—	{	{	+	—	CDe/CDE CDe/Cde CDe/C ^w De C ^w De/Cde C ^w de/CDE C ^w De/C ^w De C ^w de/C ^w De	R ₁ R ₁ R ₁ R' R ₁ R ₁ ^w R ₁ ^w R' R' ^w R ₁ R ₁ ^w R ₁ ^w R' ^w R ₁ ^w	R ¹ R ¹ R ¹ r' R ¹ R ^w R ^w r' r ^w R ¹ R ^w R ^w r ^w R ^w	16.6097 0.8016 1.0539 0.0254 0.0000 0.0167 0.0000
							+	+				
							+	+				
							+	+				
							—	+				
							+	—				
							—	+				
0.2101	+	—	+	+	{	{	+	—	CDe/CDE Cde/CDE CdE/CDe CDE/CDE C ^w De/CDE CdE/CDE CdE/C ^w De C ^w de/CDE	R ₁ R ₂ R'R ₂ R _y R ₁ R ₂ R ₂ R ₁ ^w R ₂ R _y R ₂ R _y R ₁ ^w R' ^w R ₂	R ¹ R ₂ r'R ₂ r _y R ¹ R ₂ R ₂ R ^w R ₂ r _y R ₂ r _y R ^w r ^w R ₂	0.1985 0.0048 0.0000 0.0006 0.0062 0.0000 0.0000 0.0000
							+	+				
							+	—				
							+	+				
							+	—				
							—	+				
							+	+				
							+	+				
0.0000	+	—	—	+	{	{	+	+	CdE/Cde CdE/CdE CdE/C ^w de	R _y R' R _y R _y R _y R' ^w	r _y r' r _y r _y r _y r ^w	0.0000 0.0000 0.0000
							+	—				
							+	+				

WIENER's antisera notation (1949): anti-C = anti-rh', anti-c = anti-hr', anti-D = anti-Rh₀, anti-E = anti-rh'', anti-C^w = anti-rh^w, anti-e = anti-hr'', anti-d = anti-Hr₀.

The blood group systems Lutheran, Kell, Lewis and Duffy have only recently been discovered but their existence may be considered as firmly established. On the other hand, their inheritance has not yet been fully explained, although it is certain that they are

independent of the blood groups which have already been described (ABO, MNSs, Pp, Rh) and that they are moreover independent of each other. There exists, however, a genetical relation ship between the blood group Lewis and the secretor/non-secretor system.

Blood group system Lutheran

Discovered by CALLENDER and RACE¹ (1946) in a patient who had received many blood transfusions and named after the donor whose blood contained the sensitizing antigen, this blood group, like the blood group Pp, is characterized by the presence of 2 genes, the (presumably) dominant Lu^a and the (presumably) recessive Lu^b. Only Lu^a forms a phenotypically occurring antigen, Lu(a⁺);

the phenotype Lu^b therefore simply denotes absence of Lu^a, hence also the designation of the phenotypes by Lu(a⁺) and Lu(a⁻). Only Lu(a⁻) forms an antibody, anti-Lu^a, and this only on immunization by incompatible blood; preformed antibodies anti-Lu^a have not yet been found.

Genes	Frequency ²	Genotypes	Frequency ^{2a}	Phenotypes	Frequency ^{2a}	Antibodies
Lu ^a	3.90%	Lu ^a Lu ^a	0.15%	} Lu(a ⁺)	7.65%	none
		Lu ^a Lu ^b	7.50%			
Lu ^b	96.10%	Lu ^b Lu ^b	92.35%	Lu(a ⁻)	93.35%	Anti-Lu ^a

Blood group system Kell

Discovered by COOMBS et al.³ (1946) in a woman immunized by an incompatible pregnancy, this blood group is characterized by the presence of 2 genes, the dominant K and the recessive k. According to the gene combination present, the phenotypically occurring antigen K⁺ or K⁻ is produced, and on immunization the corresponding antibody anti-k or anti-K. The antibodies are not preformed and have been found exclusively in women im-

munized by incompatible pregnancy⁴⁻⁷ or in persons who have received many blood transfusions^{8, 9}. Anti-K is the more strongly acting antibody and can cause severe reactions. The antigen K⁻ (phenotype kk) was discovered independently of antigen K⁺ by LEVINE et al.⁶ in 1949 and originally described as Cellano⁺; it was later identified as K⁻ by the same workers⁷.

Genes	Frequency ²	Genotypes	Frequency ^{2a}	Phenotypes	Frequency ^{2a}	Antibodies
K	5.22%	KK	0.27%	} K ⁺	10.17%	Anti-k
		Kk	9.90%			
k	94.78%	kk	89.83%	K ⁻	89.83%	Anti-K

Blood group system Lewis

This system was discovered by MOURANT¹⁰ in 1946 and named after one of the 2 donors whose blood contained the new antibody. The genetical structure has not yet been fully explained, hence the designation of the genes by Le^a and Le^b (^{10,11}). There

is a genetical relationship between the Lewis and secretor/non-secretor systems in that all Le^b-negative persons are ABO-secretors and all Le^a-negative persons non-secretors^{14, 15}.

Genes	Frequency ¹²	Genotypes	Frequency ¹²	Phenotypes	Frequency ¹³	Antibodies
Le ^a	43.24%	Le ^a Le ^a	18.7 %	Le(a ⁺ b ⁻)	18.7%	Anti-Le ^b
Le ^b	52.29%	Le ^a Le ^b	45.22%	} Le(a ⁻ b ⁺)	71.2%	Anti-Le ^a
Le?	4.47%	Le ^b Le ^b	27.34%			
		?	8.7%	Le(a ⁻ b ⁻)	10.6%	Anti-Le ^a , Anti-Le ^b

1) CALLENDER and RACE, *Ann. Eugen.*, **13**, 102, 1946. 2) RACE and SANGER, *Blood Groups in Man*, 2nd ed., Oxford, 1954. 2a) Calculated from 2. 3) COOMBS et al., *Lancet*, **1**, 264, 1946. 4) SANGER et al., *Rev. Hémat.*, **4**, 32, 1949. 5) DUNSFORD, L., *Nature (Lond.)*, **163**, 962, 1949. 6) LEVINE et al., *Science*, **109**, 464, 1949. 7) LEVINE et al., *Blood*, **4**, 869, 1949. 8) WIENER and SONN-GARDON, *Rev. Hémat.*, **2**, 1, 1947. 9) COLLINS et al., *Brit. med. J.*, **1**, 1297, 1950. 10) MOURANT, A. E., *Nature (Lond.)*, **158**, 237, 1946. 11) ANDRESEN, P. H., *Acta path. microbiol. scand.*, **25**, 728, 1948. 12) PETTENKOFFER, H. J., *Naturwissenschaften*, **40**, 321, 1953. 13) GRUBB, R., *Acta path. microbiol. scand.*, **28**, 61, 1951. 14) MILLER et al., quoted by ROSENFELD and VOGEL, *J. Mt Sinai Hosp.*, **20**, 89, 1953. 15) GRUBB, R., *Nature (Lond.)*, **162**, 933, 1948.

Blood group system Duffy

This system was discovered by CUTBUSH et al.¹ in 1950 (anti-Fy^a) through a haemophiliac who had already received several transfusions. The factor Fy^b was found in 1951 by PETTENKOFER et al.² with the aid of an agglutinin found in the routine post-natal examination of the serum of a woman delivered of her third

healthy child. The Duffy system is characterized by 2 genes Fy^a and Fy^b and is of clinical significance in the case of reactions shown by patients who have received many transfusions. The Duffy antibodies are mostly identifiable only by means of anti-human globulin solution (COOMBS test, see page 343).

Genes	Frequency ³	Genotypes	Frequency ³	Phenotypes	Frequency ³	Antibodies
Fy ^a	41.65%	Fy ^a Fy ^a	17.35%	Fy(a ⁺ b ⁻)	17.35%	Anti-Fy ^b
		Fy ^a Fy ^b	48.60%	Fy(a ⁺ b ⁺)	48.60%	none
Fy ^b	58.35%	Fy ^b Fy ^b	34.05%	Fy(a ⁻ b ⁺)	34.05%	Anti-Fy ^a

Blood group system Kidd

This system was discovered by ALLEN et al.⁵ in 1951 through the identification of the factor Jk^a in the serum of the mother of an

erythroblastic child. In 1953 PLAUT et al.⁶ found the anticipated antibody anti-Jk^b which identifies the allelomorphic antigen Jk^b.

Genes	Frequency ⁷	Genotypes	Frequency ⁷	Phenotypes	Frequency ⁷	Antibodies
Jk ^a	52.8%	Jk ^a Jk ^a	27.8%	Jk(a ⁺ b ⁻)	27.8%	Anti-Jk ^b
		Jk ^a Jk ^b	50.0%	Jk(a ⁺ b ⁺)	50.0%	none
Jk ^b	47.2%	Jk ^b Jk ^b	22.2%	Jk(a ⁻ b ⁺)	22.2%	Anti-Jk ^a

Blood group system Jay

This group was discovered by LEVINE et al.⁸ in 1951 through an antibody, anti-Tj^a, found in the serum of a carcinoma patient. Subsequently the same antibody was identified in other sera by workers in South Africa, Australia, Europe and Japan. Anti-Tj^a serum reacts positively with almost all European and Japanese blood samples. Only the antibody carriers and possibly their relatives re-

act negatively (hereditary character). A close relationship between this system and the P system has recently been established^{9a}. The Jay system has at present no clinical importance since the antibodies are probably preformed and the discovery of a donor is very unlikely in view of the frequency of positive reactions.

Secretor/non-secretor system

This system was discovered by LEHRS⁹ and PUTKONEN¹⁰ in 1930 and a genetical theory has been put forward by SCHIFF and

SASAKI¹¹. It is characterized by 2 genes, S (dominant) and s (recessive). Cf. also remarks on page 341.

Genes	Frequency ¹²	Genotypes	Frequency ^{12a}	Phenotypes	Frequency ^{12a}
S	55.2%	SS	30.58%	} S (secretor)	79.92%
		Ss	49.34%		
s	44.8%	ss	20.08%	s (non-secretor)	20.08%

There is a genetical relationship between this system and the blood group Lewis (see the opposite page).

¹) CUTBUSH et al., *Nature (Lond.)*, 165, 188, 1950. ²) IKIN, MOURANT, PETTENKOFER and BLUMENTHAL, *Nature (Lond.)*, 168, 1077, 1951. ³) HOLLAENDER, Li., *Acta Haematol.*, 6, 257, 1951 (417 cases in Switzerland, in good agreement with CUTBUSH¹ and BLUMENTHAL and PETTENKOFER²). ⁴) BLUMENTHAL and PETTENKOFER, *Z. Immunforsch.*, 109, 267, 1952. ⁵) ALLEN et al., *Nature (Lond.)*, 167, 482, 1951. ⁶) PLAUT et al., *Nature (Lond.)*, 171, 431, 1953. ⁷) ROSENFELD and VOGEL, *J. Mt Sinai Hosp.*, 20, 89, 1953. ⁸) LEVINE et al., *Proc. Soc. exp. Biol.*, 77, 403, 1951 (cf. also LEVINE, P., *Tr. N. Y. Acad. Sci.*, 13, 205, 1951). ^{9a}) SANGER, R., *Nature*, 176, 1163, 1955. ⁹) LEHRS, H., *Z. Immunforsch.*, 66, 175, 1930. ¹⁰) PUTKONEN, T., *Acta Soc. Med. "Duodecim"*, 14, quoted by RACE and SANGER, *Blood Groups in Man*, 2nd ed., Oxford, 1954. ¹¹) SCHIFF and SASAKI, *Z. Immunforsch.*, 77, 129, 1932. ¹²) Mean of the values given by the following six authors: GRUBB and MORGAN, *Brit. J. exp., Path.*, 30, 198, 1949; HARTMANN, G., *Group Antigens in Human Organs*, Copenhagen, 1941; MORZYCKY, G., *C. R. Soc. Biol.*, 115, 658, 1934; PUTKONEN¹⁰; SCHIFF, F., *Amer. J. phys. Anthropol.*, 27, 255, 1940; WIENER, A. S., *Blood Groups and Transfusion*, 3rd ed., Springfield, 1943. ^{12a}) Calculated from ¹².

Synopsis of Cerebrospinal Fluid
(Values in mg/100 ml, unless otherwise stated)

Lumbar fluid	Normal	Abnormal	Methods* and bibliography	Remarks
Appearance	Bright, clear	Possibly cloudy, opalescent	Cell count by means of counting chamber. Nature of cells and bacteria in the centrifuged sediment.	Cloudiness starts at a cell count of 200 to 300 or may be due to bacteria or to both. Normal cell count (usually lymphocytes) 0-5 per mm ³ , values over 10 almost always pathological.
	No coagulum . . .	Possible coagulum		Usually forms when the protein content exceeds 100 mg. The coagulum is usually richer in cells and bacteria.
Quantity	100-150 ml (adults)		After MOTT, F. W., <i>Lancet</i> , 2 , 1, 1910.	This is the amount which can be removed at lumbar puncture. In the newborn it varies from a few drops to 5 ml.
Colour	Colourless	Colourless or yellow, pale red to red	Bilirubin: VAN DEN BERGH's test (see also under Blood, page 319); examination of centrifuged sediment.	The bilirubin to which the yellow coloration is due is usually the result of haemorrhage (except in longstanding jaundice). Yellow colour (<i>xanthochromia</i>) often results from tumours of the spinal medulla. Yellowish colour often occurs in meningitis (regardless of aetiology), in cerebral or meningeal haemorrhage; in cerebral thromboses, tumours; in polyneuritis; in long-standing jaundice; possibly also 2-3 weeks after lumbar puncture which has caused accidental bleeding.
Pressure**				
recumbent position	100-200 mm H ₂ O 7.5-15 mm Hg	Over 200 mm	After SUNDERMAN and BOERNER, <i>Normal Values in Clinical Medicine</i> , Philadelphia, 1950.	Increased by crying, coughing, sneezing and struggling by 100 mm H ₂ O or more, so that no reliable data can be given for children.
Specific gravity	1.005-1.009 (lumbar fluid) 1.002-1.004 (ventricular fluid)			
Surface tension	62.1-65.1 dyn cm ⁻¹ (20° C); mean 63.6		Ring method of BRINKMAN and VAN DAM, after KÜNZEL, O., <i>Dtsch. Z. Nervenheilk.</i> , 139 , 265, 1936.	
Viscosity	1.020-1.027 (38° C; water = 1)		After LEVINSON, A., <i>Cerebrospinal Fluid in Health and Disease</i> , St. Louis, 1919.	
Electrical conductivity .	0.01425-0.01549 S cm ⁻¹ (25° C) ***		After ECKEL, J. L., <i>Human Cerebrospinal Fluid</i> , New York, 1926.	
Freezing-point depression	0.56-0.60° C		After LICKINT, F., <i>Z. ges. Neurol. Psychiat.</i> , 120 , 148, 1929.	Plasma and spinal fluid are isotonic within ca. 2 mmol (a freezing-point depression of 0.56° C corresponds to a tonicity, i.e. total concentration of osmotically active particles, of 301.4 mmol/1000 g H ₂ O). This small difference is due to the protein content of plasma (the concentration of all other osmotically active particles is the same in both fluids).
Hydrogen-ion concentration	pH 7.25-7.42; mean 7.35		After REICHNER, H., <i>Z. ges. Neurol. Psychiat.</i> , 123 , 436, 1930.	
Refractive index	1.33494-1.33510		After HALLMANN, L., <i>Klinische Chemie und Mikroskopie</i> , Stuttgart, 1950.	
Proteins				
Total	10-25 Ventricular fluid contains significantly less protein than lumbar fluid	Over 30 is suspicious, over 35 definitely pathological. The KJELDAHL method gives higher values than turbidity tests. According to MERRITT and FREMONT-SMITH, <i>Cerebrospinal Fluid</i> , Philadelphia, 1937, normal values for adults are 15-45 mg.	Accurate determination: micro-KJELDAHL or after WU, H., and LING, S. M., <i>Chin. J. Physiol.</i> , 1 , 161, 1927. See also 'under Blood, page 313. For a summary see LINDENMEYER, E., <i>Mtschr. Psychiat. Neurol.</i> , 109 , No. 2, 1944.	The ratio of total protein contents spinal fluid : plasma is ca. 1:400. Very greatly increased in cerebral haemorrhage and thrombosis, often also in cerebral abscesses and tumours. Always greatly increased in coccal meningitis, esp. that due to meningococcus. Often greatly increased in tuberculous and typhic meningitis; in poliomyelitis (in 2nd week). Moderately increased in influenza meningitis; in meningeal haemorrhage; in secondary syphilis and progressive paralysis. Slightly increased or unchanged in congenital syphilis; in tabes; in encephalitis lethargica; in poliomyelitis in preparalytic stage and during the first week; in multiple sclerosis, syringomyelia, herpes zoster. (After GREENFIELD, J. G., and CARMICHAEL, E. A., <i>The Cerebrospinal fluid in Clinical Diagnosis</i> , New York, 1925.)
Electrophoretic fractions as percentage of total proteins				
Fraction V	4.3 Fraction V is a precursor of albumins.	By paper electrophoresis. Values from GRIES et al., <i>Klin. Wschr.</i> , 31 , 644, 1953.	
Albumins	51.3			
Globulins a ₁	5.8			
a ₂	8.4			
β	17.1			
τ	6.8			
γ	6.3			

* See also KAFKA, V., *Taschenbuch der praktischen Untersuchungsmethoden der Körperflüssigkeiten bei Nerven- und Geisteskrankheiten*, 5th ed., Basle, 1948.
** QUECKENSTEDT test: Normally the cerebrospinal fluid pressure rises when both jugular veins are compressed, the rise quickly disappearing when the pressure is released. Increase of pressure when one jugular vein is compressed indicates an obstruction or thrombosis of the lateral sinus on the opposite side.
*** S cm⁻¹ = siemens × cm⁻¹ = ohm⁻¹ × cm⁻¹.

(Values in mg/100 ml, unless otherwise stated)

Lumbar fluid

Proteins (continued)	Normal	Abnormal	Methods* and bibliography	Remarks
Albumins	~ 20	Values from HEWITT, L. F., <i>Brit. J. exp. Path.</i> , 8 , 84, 1927. Globulin tests: PANDY's test; NONNE-APELT test; gold-sol test of LANGE et al., <i>Amer. clin. Path.</i> , 20 , 872, 1950.	Ratio albumins/globulins: (a) usual in acute affections; (b) usual in chronic affections. These tests are also a criterion of the total protein content (in PANDY's test positive at ca. 30 mg, in NONNE-APELT test at ca. 50 mg) although primarily they indicate a pathological increase in globulins. The gold-sol test is specific for pathological changes in the albumin/globulin ratio: it yields characteristic flocculation curves, e.g. in meningitis, secondary syphilis, progressive paralysis, tabes.
Globulins	~ 3		
Ratio albumins/globulins.	~ 8 : 1	{ (a) 12 : 1 (b) 0.9 : 1 }		
Amino-acid nitrogen ..	1.2-2	After WIECHMANN and DOMINICKE, <i>Dtsch. Arch. klin. Med.</i> , 153 , 1, 1926.	
Urea	10-40	over 40	As in blood serum (see under Blood, page 317).	The urea content is lower than that in plasma but normally rises and falls with the latter content. No particular diagnostic significance.
Creatinine	0.54-1.91	After COCKRILL, J. R., <i>Arch. Neurol. Psychiat.</i> , 25 , 1297, 1931.	
Non-protein nitrogen ..	12-44	Amino-acids + creatinine + urea.
Reducing substances	The reducing substances of spinal fluid consist almost entirely of glucose (see also under Urine and Blood). While the content in ventricular fluid is roughly the same as that in plasma, the glucose content of lumbar fluid is lower but normally rises and falls with the blood sugar content (cf. the comparative values for lumbar and ventricular fluids on the next page). <i>The sugar content is usually lowered in coccal and typhic meningitis (down to zero); in influenzal meningitis; in acute secondary syphilis; in progressive paralysis. Often increased in virus meningitis (mumps); in brain abscesses, tumours and haemorrhages; in congenital syphilis, tabes; in polyneuritis; in poliomyelitis; in encephalitis lethargica and kidney diseases, arteriosclerosis and diabetes (after GREENFIELD, see under Proteins above).</i>
"Total sugar"	45-100	{ under 45 over 100 }	See under Blood, page 320.	
Qualitative test	positive	{ negative strongly positive }	FEHLING's test, see under Urine, page 289.	
Reducing substances other than glucose	~ 4	
Pyruvic acid	mean 0.905	20 cases. After LASCH, F., <i>Klin. Wschr.</i> , 39 , 941, 1953. In agreement with AMATUZIO and NESBITT, <i>J. clin. Invest.</i> , 29 , 1486, 1950.	
Lactic acid	9-15	After KAFKA, V., <i>Die Cerebrospinalflüssigkeit</i> , Leipzig and Vienna, 1930.	
Cholesterol	0.06-0.22	After PLAUT and RUDY, <i>Z. ges. Neurol. Psychiat.</i> , 146 , 229, 1933.	
Chlorides (as NaCl)	700-760	{ under 700 over 760 }	See under Blood, page 326.	The NaCl content of spinal fluid, unlike the glucose and urea contents, is higher than that of plasma but normally rises and falls in proportion to the plasma NaCl content. <i>Not increased in any form of syphilis, mumps meningitis or cerebral haemorrhages, tumours or abscesses. Other fluctuations (increases, etc.) as for sugar.</i>
Sodium (mg. equiv/l).	142.47	}	100 cases. Determined by flame photometry. After SHAW and HOLLEY, <i>J. Lab. clin. Med.</i> , 38 , 574, 1951.	No pathological changes (MOND, W., <i>Klin. Wschr.</i> , 30 , 87, 1952).
(mg)	327.5			
Potassium (mg. equiv/l).	2.88			
(mg)	11.80			
Iodine	0.58 µg	After EVERETT, M. R., <i>Medical Biochemistry</i> , New York, 1946.	
Carbon dioxide combining capacity	40-60 vol%	After SUNDERMAN and BOERNER, <i>Normal Values in Clinical Medicine</i> , Philadelphia, 1950.	
(bicarbonate CO ₂)				

* See also KAFKA, V., *Taschenbuch der praktischen Untersuchungsmethoden der Körperflüssigkeiten bei Nerven- und Geisteskrankheiten*, 5th ed., Basle, 1948.

Chemical composition of lumbar fluid compared with that of plasma¹
(Normal values)

		mg/100 ml		Ionic equivalents mg. equiv/l	
		Lumbar fluid	Plasma	Lumbar fluid	Plasma
Sodium	Na	325	325	141	141
Potassium	K	10	20	2.5	5
Calcium	Ca	5	10	2.5	5
Magnesium	Mg	3	3	2	2
Total cations		—	—	148	153
Chlorine	Cl	449	360	126.5	101
HCO ₃ (vols. CO ₂)	40	60	18	27
Phosphorus	P	2	3	1	2
Sulphur	S	0.5	1	0.5	1
Organic acids	trace	trace	2	2
Proteins	30	7000	negligible	20
Total anions		—	—	148	153
Urea	24	30	4	5
Sugar	72	90	4	5
Total equivalents		—	—	304	316

Sugar content of blood compared with that of lumbar, cisternal and ventricular fluids²
Values in mg/100 ml

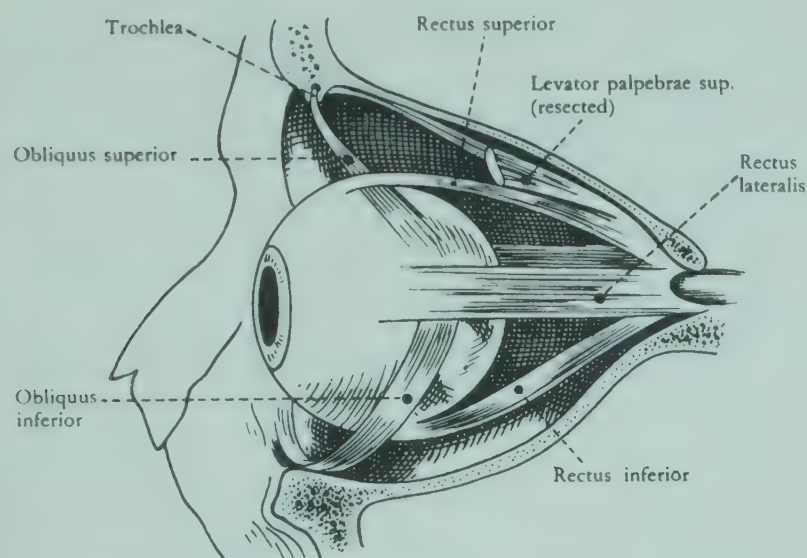
Blood	Lumbar fluid	Cisternal fluid	Ventricular fluid
200	100	112	196
195	100	150	175
175	93	100	175
148	93	100	150
143	93	100	137
125	86	93	121
112	86	86	106
106	86	86	100
100	93	93	137

The ventricular fluid has a lower specific gravity than the lumbar fluid and is also practically free of proteins and cellular constituents.

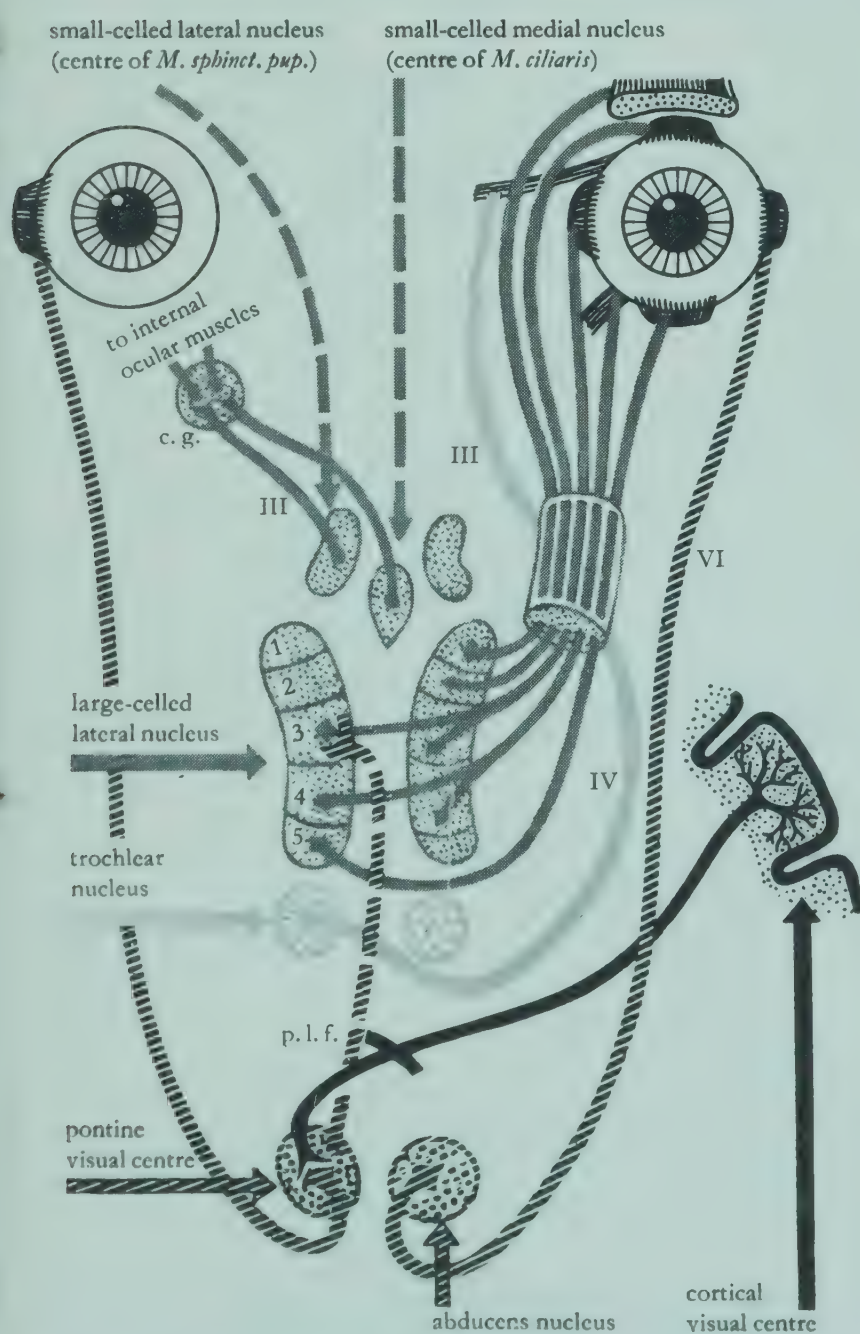
¹⁾ After HARRISON, G. A., *Chemical Methods in Clinical Medicine*, London, 1947, page 423.
²⁾ After CHEVASSUT, K., *Quart. J. Med.*, 21, 91, 1927.

By Dr. med. ALFRED HUBER, University Ophthalmological Clinic, Zurich (Director, Prof. MARC AMSLER)

Orbit and ocular muscles



Lateral view of the orbit and ocular muscles



- III = Oculomotor nerve
 IV = Trochlear nerve
 VI = Abducens nerve
 c.g. = Ciliary ganglion
 p.l.f. = Posterior longitudinal fasciculus
- 1 = Centre of the *M. levator palpebrae superioris*
 2 = Centre of the *M. rectus superior*
 3 = Centre of the *M. rectus medialis*
 4 = Centre of the *M. obliquus inferior*
 5 = Centre of the *M. rectus inferior*

Innervation of the ocular muscles

(after BING, R., *Gehirn und Auge*, Basle, 1954)

Functions of the ocular muscles

Muscle	Nerve	Lateral action	Vertical action	Rotation
Rectus medialis	III	adduction	—	—
Rectus lateralis	VI	abduction	—	—
Rectus superior (left)	III	adduction	upwards	counter clockwise
Rectus inferior (left)	III	adduction	downwards	clockwise
Obliquus superior (left)	IV	abduction	downwards	counter clockwise
Obliquus inferior (left)	III	abduction	upwards	clockwise

Clinical symptoms of pareses of the individual ocular muscles

Lateral rectus (*abducens nerve*)Example: Paresis or paralysis of the left *rectus lateralis*

1. Slight convergence of the left eye
2. Angle of strabism increases when sight is directed to the left
3. Uncrossed diplopia when sight is directed to the left, with increasing separation of the images in the leftward direction
4. Head turned slightly to the left

Medial rectus (*oculomotor nerve*)Example: Paresis or paralysis of the right *rectus medialis*

1. Slight divergence of the right eye
2. Angle of strabism increases when sight is directed to the left
3. Crossed diplopia when sight is directed to the left, with increasing separation of the images in the leftward direction
4. Head turned slightly to the left

Superior rectus (*oculomotor nerve*)Example: Paresis or paralysis of the left *rectus superior*

1. Left eye rotated downwards
2. Angle of strabism increases when sight is directed upwards and to the left
3. Vertical diplopia; left image above the right
4. Head slightly inclined towards the right shoulder

Inferior rectus (*oculomotor nerve*)Example: Paresis or paralysis of the right *rectus inferior*

1. Right eye rotated upwards
2. Angle of strabism increases when sight is directed downwards and to the right
3. Vertical diplopia; right image below the left
4. Head slightly inclined towards the right shoulder

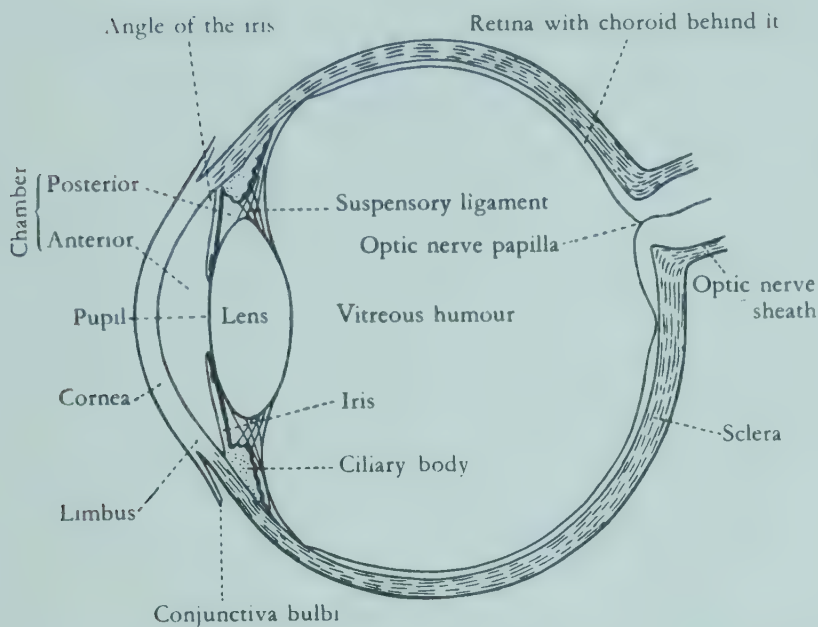
Inferior oblique (*oculomotor nerve*)Example: Paresis or paralysis of the right *obliquus inferior*

1. Right eye rotated downwards
2. Angle of strabism increases when sight is directed upwards and to the left
3. Vertical diplopia; right image above the left. Diplopia increases when sight is directed upwards and to the left upwards
4. Head inclined slightly backwards and towards the right shoulder

Superior oblique (*trochlear nerve*)Example: Paresis or paralysis of the left *obliquus superior*

1. Left eye rotated slightly upwards. Deflection increases when sight is directed downwards and to the right downwards
2. Vertical diplopia with simultaneous reciprocal lateral rotation of the images. Diplopia increases when sight is directed downwards and to the right downwards
3. Head markedly inclined towards the right shoulder (principal characteristic of paralysis of the *obliquus superior*)

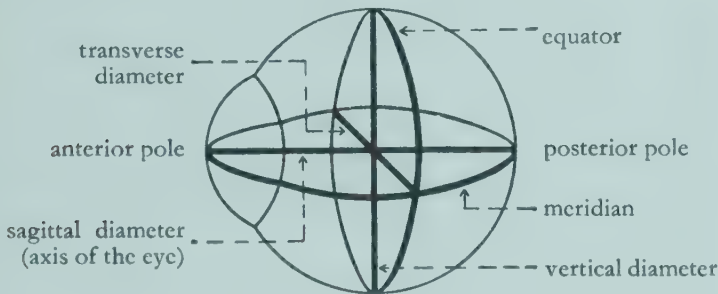
Schematic cross-section through the eyeball



The eye is composed of three coats :

- I. Protective coat: Cornea-sclera and conjunctiva
- II. Nutritional coat: Choroid-ciliary body and iris
- III. Light-sensitive coat: Retina

Dimensions of the eyeball



Diameter (millimetres)	Mean	Normal range
Adults		
sagittal	24.26 ¹	23.85 –25.0 ²
transverse	23.90 ³	23.0 –24.5 ⁴
vertical	23.85 ⁵	23.0 –23.7 ⁶
Newborn		
sagittal	17.15 ⁷	16.4 ⁸ –17.9 ⁹
transverse	17.15 ⁷	16.0 –18.3 ⁹
vertical	15.4 ⁸	
Circumference (equator) (mm) ...	73.8 ¹⁰	72.2 ¹¹ –78 ¹²
Volume (cubic centimetres)		
Adults	7.180 ^{13a}	–
Newborn	2.185 ¹⁴	–

(Eyeball)		
Weight (grams)	Mean	Normal range
Adults	7.448 ^{18b}	–
Newborn	2.290 ¹⁴	–
Specific gravity	1.036 ¹⁵	1.02–1.09 ¹⁶

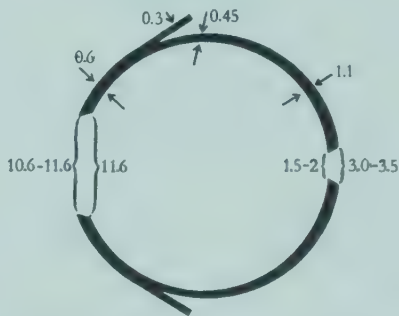
Elements of the eyeball

I. Protective coat

A. Sclera

Thickness (millimetres)	Mean	Normal range
at the fundus (posterior pole) ..	1.1 ¹⁷	1 –1.2 ¹⁸
at the equator	0.45 ¹⁷	0.4–0.5 ¹⁸
at the limbus	0.6 ^{17,18}	–

Thinner in children than in adults, thinner in women than in men.



Diameter of the anterior scleral aperture (mm)	10.6–11.6 ¹⁶
Diameter of the posterior scleral aperture	
internal	– 1.5– 2.0 ¹⁶
external	– 3.0– 3.5 ¹⁶

B. Cornea

Thickness (in vivo, millimetres)¹⁹

	20°	nasal 10°	5°	central	5°	temporal 10°	20°
Women:	0.6590	0.6192	0.5527	0.5527	0.5529	0.6193	0.6592
Men:	0.6590	0.6062	0.5399	0.5131	0.5399	0.6063	0.6591

Diameter (millimetres) ¹⁶ (determined by means of the WESSELY keratometer)	Mean	Normal range
horizontal	11.6	–
vertical	10.6	–

Radius of curvature (millimetres) (determined optically with the JAVAL-SCHIÖTZ ophthalmometer)	Mean	Normal range
Anterior surface	7.84 ²⁰	7.7 ²¹ –7.98 ²²
Posterior surface	6.51 ²⁰	6.22 ²² –6.8 ²¹

Physiological astigmatism (diopters) ¹⁶ (Difference of corneal radii of curvature in horizontal and vertical meridian; more strongly refracting vertically than horizontally in 89.4% of cases)	Mean	Normal range
Index of refraction ²³	1.3763	–

1) Calculated from 11 mean values (standard deviation $\sigma = 0.41$ mm) taken from the following authors: EMMERT, *Z. vergl. Augenheilk.*, **4**, 40, 1886; MERKEL-KALLIUS, *Anatomic des Auges*, in *Handbuch der gesamten Augenheilkunde*, 2nd ed., Leipzig, 1910; QUAIN, *Elements of Anatomy*, 1894; RAUBER, *Anatomic des Menschen*, Leipzig, 1893; ROCHON-DUVIGNEAUD, *Bull. Biol. France-Belgique*, **54**, 109, 1921; SAPPEY, *Gaz. méd.*, **10**, 408, 1855; SALZMANN, *Anatomic und Histologie des menschlichen Augapfels*, Leipzig, 1912; SCHWALBE, *Anatomic des Auges*, Leipzig, 1887; SLONAKER, J. R., *J. Morph.*, **31**, 351, 1918; VOLKMANN, *Sitz. G. d. W. Leipzig math.-phys. Kl.*, **21**, 30, 1869; WALLS, *J. comp. Neurol.*, **46**, 465, 1928; WEISS, L., *Anat. Hefte*, **25**, 191, 1897. 2) Minimum and maximum values from 1. 3) Calculated from 9 mean values (standard deviation $\sigma = 0.57$ mm) taken from the following authors: EMMERT, MERKEL-KALLIUS, QUAIN, RAUBER, SAPPEY, SALZMANN, SCHWALBE, VOLKMANN, WALLS (for references see under 1). 4) Minimum and maximum values from 3. 5) Calculated from 9 mean values (standard deviation $\sigma = 0.24$ mm) taken from the following authors: EMMERT, MERKEL-KALLIUS, QUAIN, RAUBER, SAPPEY, SALZMANN, SLONAKER, WALLS, WEISS (for references see under 1). 6) Minimum and maximum values from 5. 7) Mean value from 8 and 9. 8) WEISS, *Anat. Hefte*, **25**, 191, 1897. 9) v. PFLUCK, *Klin. Mbl. Augenheilk.*, **47**, 1, 1909. 10) Calculated from 4 mean values from the following authors: MERKEL-KALLIUS, SALZMANN, WEISS (for references see under 1) and SCHNABEL, *Z. Heilk.*, **16**, 1, 1895. 11) SALZMANN, *Anatomic und Histologie des menschlichen Augapfels*, Leipzig, 1912. 12) SCHNABEL, *Z. Heilk.*, **16**, 1, 1895. 13) a and b, WEISS, L., *Anat. Hefte*, **25**, 191, 1897. 14) STEINDORFF, K., *Tab. biol.*, (Amst.), **22**, (1), 166, 1947. 15) Calculated from 13 a and b. 16) DUKE-ELDER, W. S., *Textbook of Ophthalmology*, Vol. I, London, 1932. 17) HEINE, L., *Jena Z. Naturw.*, **41**, 612, 1905. 18) HOTTA, G., *Arch. Ophthal.*, **62**, 253, 1906. 19) SOBANSKI, *Klin. oczna*, **21**, 317, 1914. 20) Calculated from 21 and 22. 21) GULLSTRAND, quoted by DUKE-ELDER 16. 22) TSCHERNING, quoted by DUKE-ELDER 16. 23) MATHIESSEN, quoted by DUKE-ELDER 16.

II. Nutritional coat

A. Choroid

Thickness (millimetres)

at the ora serrata	0.1–0.15 ¹
at the fovea	0.22 ²

(The ora serrata is located 8 mm from the limbus)

B. Ciliary body

(a circular band behind the iris)

Width of this band (millimetres)

nasal and above	4.6–5.2 ¹
temporal and below	5.6–6.3 ¹
consists of: pars plana	3.6–4 ³
pars plicata	2 ³

Thickness (millimetres) 1.0–1.5⁴

The ciliary body contains the **ciliary muscle** (*M. ciliaris*, length 2.3–6.4 mm, thickness 0.5–0.6 mm)⁵. This muscle is responsible for **accommodation** by changing the radius of curvature of the lens:

Accommodation and near-point of the emmetropic eye as a function of age			
Age (Years)	Near-point (in cm)	Accommodation (in diopters)	Presbyopia correction (in diopters)
10	7	14	
20	9	11	
30	12	8	
40	22	4.5	
45	28	3.5	
50	40	2.5	0.75–1.0
55	55	1.75	1.0 –1.5
60	100	1.0	2.0 –2.5
65	133	0.75	3.0 –3.5
70	400	0.25	3.5 –4.0
75	infinity	0	

(Tables for near-vision testing will be found in the pocket inside the back cover.)

C. Pupil

Inter-pupillary distance (millimetres)⁶

	male	female
Adults (Switzerland)	63	61
Children (Switzerland)		
4 years	49	47
10 years	55	55
15 years	59	58

Pupillary diameter

The diameter of the pupil is controlled by the antagonistic actions of the *M. dilatator pupillae* and the *M. sphincter pupillae*. The *M. dilatator pup.* is sympathetically innervated (from the first three cervical ganglia located over the plexus of the internal carotid); the *M. sphincter pup.* and the ciliary muscle are parasympathetically innervated (from the ciliary ganglion). This simple reciprocal innervation plan is shown to be somewhat more complicated on critical study with various drugs⁷. It suffices, however, for clinical purposes (see visual path, diagram, page 360).

The diameter of the pupil appears to be increased by 10–12.5% as a result of the curvature of the cornea^{8, 9}.

The average diameter of the pupil depends upon age:

Age	Diameter ¹⁰ (millimetres)	Age	Diameter ¹¹ (millimetres)
Newborn	2.5–3.25	3–23 years	3
1 month	1.5	23–28 years	2.833
1–5 months	1.858	28–38 years	2.666
6–9 months	2.266	38–53 years	2.50
10–30 months	2.653	53–81 years	2.33
2½–6 years	2.914		
6–12 years	3.204		

The *actual pupillary diameter*, in accordance with the innervation of the *M. dilatator pup.* and the *M. sphincter pup.* described, is dependent upon the vegetative tonus (ratio of the sympathetic [adrenergic] to the parasympathetic [cholinergic] tonus). Stimulation of the sympathetic (or suppression of the parasympathetic) results in active (or passive) dilatation (mydriasis); stimulation of the parasympathetic (or suppression of the sympathetic) results in active (or passive) contraction (miosis) of the pupil.

Effect of various drugs on the pupil^{7, 12}

Myotics	Mydriatics
Sympathicolitics (<i>anti-adrenergics, passive contraction</i>): ergotamine, ergotoxin (only in large doses, small doses cause dilatation).	Sympathomimetics (<i>adrenergics, active mydriasis</i>): adrenaline, ephedrine (the latter only in Caucasians, not in Ethiopians, intermediate action in Mongolians), cocaine and its derivatives.
Cholinergics (<i>active contraction combined with spasm of the M. ciliaris: accommodation to near vision</i>): acetylcholine, pilocarpine, alkyl phosphates, e.g. tetraethyl pyrophosphate; cholinergics, by virtue of their protective action against, or destructive action on, cholinesterase : DFP (diisopropyl fluorophosphate*, physostigmine** (eserine), prostigmine**.	Anticholinergics (<i>passive mydriasis combined with paralysis of the M. ciliaris: accommodation to distant vision</i>): atropine, scopolamine, homatropine and other atropine derivatives.
<div>* destroys cholinesterase irreversibly</div> <div>** reversibly</div>	Without paralysis of the <i>M. ciliaris</i> : eucatropine (4-mandeloxy-1:2:2:6-tetramethylpiperidine).

Of toxicological significance:

Morphine (central action) histamine, muscarine, barbiturates (at the beginning of the intoxication, later hippus due to changing CO ₂ concentration).	Alcohol (central action), muscaridine, bearded darnel (<i>Lolium temulentum</i>).
------------------------------------------------------------------------------------------------------------------------------------------------------------------	-------------------------------------------------------------------------------------

¹) SALZMANN, W., *Anatomie und Histologie des menschlichen Augapfels*, Leipzig, 1912. ²) EDINGER, T., *Zool. Jb. Anat.*, **51**, 163, 1929. ³) DUKE-ELDER, W. S., *Text-book of Ophthalmology*, Vol. I, London, 1932. ⁴) EISLER, P., in SCHIECK and BRÜCKNER, *Kurzes Handbuch der Ophthalmologie*, Vol. I, Berlin, 1930. ⁵) LAUBER, H., in *Handbuch der gesamten Augenheilkunde*, 2nd ed., Leipzig, 1910. ⁶) STEIGER, N., in MARTIN, *Lehrbuch der Anthropologie*, Jena, 1928. ⁷) KRANTZ and CARR, *Pharmacological Principles of Medical Practice*, 2nd ed., Baltimore, 1951. ⁸) BING, R., in SCHIECK and BRÜCKNER, *Kurzes Handbuch der Ophthalmologie*, Vol. 6, Berlin, 1931. ⁹) HESS, C., in *Handbuch der gesamten Augenheilkunde*, 2nd ed., Leipzig, 1910. ¹⁰) BARTELS, Z. *Augenheilk.*, **12**, 638, 1904. ¹¹) TANGE, *Arch. Augenheilk.*, **46**, 49, 1903. ¹²) FÜHNER, H., *Medizinische Toxikologie*, 3rd ed., Stuttgart, 1951.

Pupil (continued)

Physiological reactions of the pupil

Under normal conditions (constant illumination and convergence) the pupillary diameter oscillates with a maximum amplitude of 1 mm and a frequency of 30–120 oscillations per minute¹.

Some physiological reactions of the pupil¹

Contraction	Dilatation
Adduction of the eyes (convergence to near vision)	Abduction of the eyes (change from near to distant vision)
Increase in light intensity	Decrease in light intensity
Deep expiration	Deep inhalation
During sleep (proportional to the soundness of sleep)	On awakening (transitory)
In the death agony, 12–24 hours after death	At the instant of death (particularly in sudden death)
Extreme fatigue	Slight fatigue
	Fright, pain, anger, orgasm, loud noises, intense odours
Imagination of bright light	Imagination of darkness

The most important of these reflexes are the *reactions to light* (or darkness) and the *convergence reaction*. For pupillary reflex path, see diagram on page 360.

Reactions to light and darkness

The **direct** light reflex (change of illumination striking both eyes) is to be distinguished from the **indirect** light reflex (change of illumination striking only one eye). In the **indirect reaction**, the covered eye normally reacts in the same manner as the exposed eye.

The *pupillomotor light adaptation time* is longer on changing from a greater to a lesser light intensity (ca. 15 minutes) than in the reverse process (ca. 4 minutes)².

Direct reaction to light (white light)

General behaviour: even *very small increases in light intensity* (from 95 to 100) suffice to cause pupillary contraction³. The *absolute value* of the intensity at which the iris begins to react is also extremely small: after total darkness an intensity of 0.01 lux is sufficient to produce a small movement in the iris; 0.025 lux causes a pupillary contraction of 0.5 mm, and 0.08 lux a contraction of 1 mm⁴. After a *latent period*⁵ of 0.21–0.22 second (independent of the initial pupillary diameter) the pupil contracts rapidly at

first, then more and more slowly. The *rate of contraction* is about 5.48 mm/second⁶ and is at first higher the greater the initial pupillary diameter⁵. The larger the initial pupillary diameter the longer is the time required to attain the *final contraction corresponding to the actual light intensity*. For any definite intensity there is a corresponding characteristic pupillary diameter¹.

Course of contraction in adaptation to bright light⁵

Time (seconds)	Pupillary diameter (millimetres)	Time (seconds)	Pupillary diameter (millimetres)
0.00	7.5	2.20	3.13
0.20	7.43	2.40	3.03
0.40	6.20	2.60	3.00
0.60	5.45	2.80	2.97
0.80	4.77	3.00	2.93
1.00	4.40	3.20	2.87
1.20	4.05	3.40	2.83
1.40	3.75	3.60	2.82
1.60	3.55	3.80	2.77
1.80	3.38	4.00	2.77
2.00	3.23	Final state of contraction after ca. 14 minutes	

Amplitude of contraction (millimetres)

Newborn ⁷	maximum	3.5
Children ⁸	1– 5 months	average 0.994
	6– 9 months	1.233
	10–30 months	1.385
	2½– 6 years	1.585
	6–12 years	1.920
Adults ⁹	generally within	0.8–2.7
		1–1.5

Direct reaction to obscuration (white light)

The dilatation of the pupil is generally inversely proportional to the light intensity¹⁰, the product dilatation × light intensity remaining constant at 0.54¹⁰ or, as elsewhere reported, 0.609¹¹.

Course of dilatation in dark-adaptation (for the light-adapted eye)¹²

Time (seconds)	Pupillary diameter (millimetres)	Time (seconds)	Pupillary diameter (millimetres)
0	2.8	15	6.5
0.5	3.1	29	6.8
1.5	3.9	60	7.2
3	4.7	180	7.5
5	5.5	300	7.6
9	6.2		

Convergence reaction (adaptation to near vision)

The contraction due to adduction of the eyes in near vision is superimposed on that due to light, the former predominating. The convergence reaction commences at a visual distance of about 40 cm and continues with increasing contraction down to a visual distance of about 20 cm. It continues as long as the convergence persists¹.

¹) NORDMANN, J., *Tab. biol. (Amst.)*, 22 (1), 298, 1947. ²) SCHIRMER, *Arch. Ophthal.*, 40, 8, 1894; *ibid.*, 44, 358, 1897. ³) GROETHUYSEN, *Arch. Augenheilk.*, 87, 152, 1920. ⁴) ENGELKING, *Z. Sinnesphysiol.*, 50, 319, 1919. ⁵) MACHEMER, *Klin. Mbl. Augenheilk.*, 94, 305, 1935. ⁶) GRADLE, *ibid.*, 71, 311, 1923. ⁷) BARTELS, *Z. Augenheilk.*, 12, 638, 1904. ⁸) PFISTER, *Arch. Kinderheilk.*, 26, 11, 1899. ⁹) WEILER, *Z. ges. Neurol. Psychiat.*, 2, 101, 1910. ¹⁰) OVIO, *Anatomie et Physiologie de l'œil, série animale*, Paris, 1927, quoted by NORDMANN¹. ¹¹) SILVESTRINI, *Ann. Ottal.*, 58, 255, 1930. ¹²) REEVES, *Psychol. Rev.*, 25, 339, 1918.

Pupil (concluded)

Relation of the pupillary diameter to light intensity and ocular convergence¹

Convergence (diopters)	Light intensity (lux)					
	0.5	1	4	10	50	200
0	5.15	4.9	4.2	3.8	3.15	2.75
1	4.3	4.0	3.7	3.4	2.95	2.6
2	3.8	3.55	3.3	3.0	2.7	2.45
3	3.75	3.2	3.0	2.8	2.5	2.3
5	3.0	2.75	2.65	2.5	2.3	2.2
7	2.7	2.6	2.45	2.3	2.2	2.1
Pupillary diameter in millimetres						

Important pupillary syndromes:

Absolute pupillary paralysis

(Lesion of sphincter nucleus or in the sphincter path)

Absence of direct and indirect reactions to light.

Absence of the convergence reaction.

Reflex pupillary paralysis (ARGYLL-ROBERTSON pupil)

(Lesion of connector neurone system)

Absence of the direct and indirect light reactions, intact convergence reaction with miosis. Anisocoria of the pupils.

ADIE's syndrome (lesion of the post-ganglionic fibres between the ciliary ganglion and sphincter muscle)

Mostly unilateral, pupil larger on affected side. Slow, tonic reaction to light (often almost absent) and convergence; also tonic relaxation of the light and convergence reactions. Occasionally also tonic accommodation.

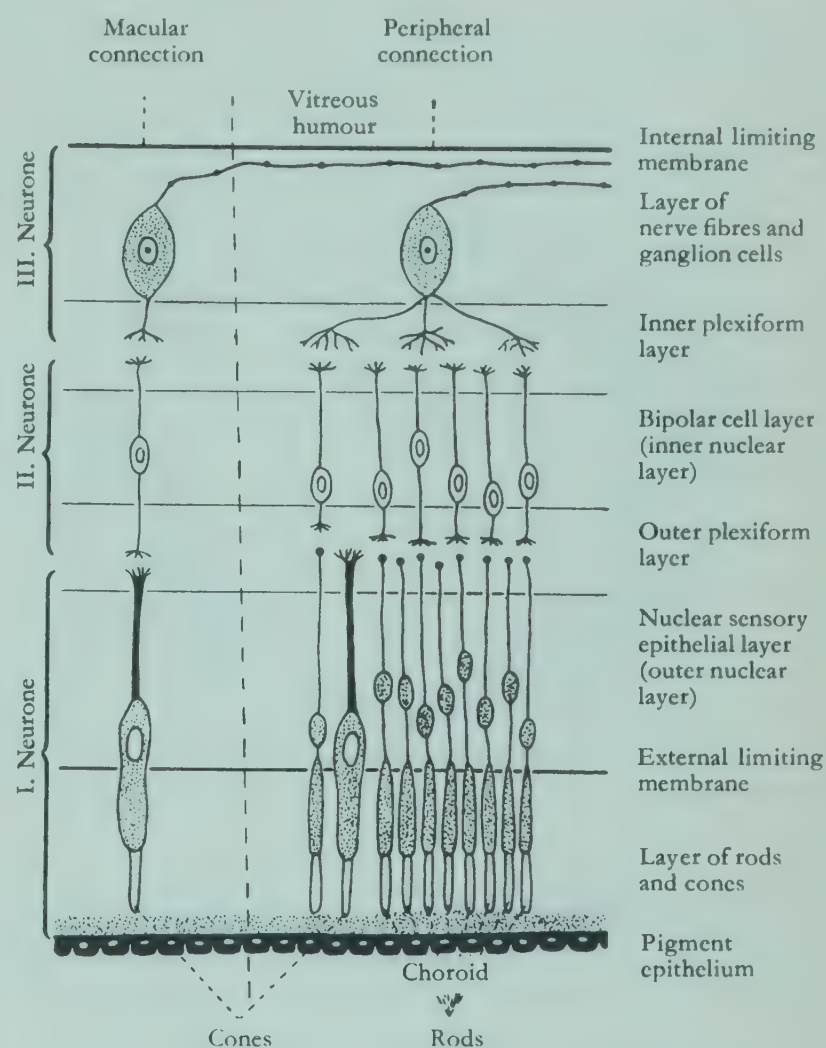
(See diagram of the pupillary reflex path on the next page.)

III. Light-sensitive coat: Retina

(Test charts for visual acuity and for colour vision will be found in the pocket inside the back cover)

Thickness (millimetres)

at the posterior pole ²	0.56
at the ora serrata ³	0.1–0.2
at the equator ³	0.2–0.3
(The ora serrata is located 8 mm from the limbus)	

Structure of the retina and its connector systems⁴

Numbers of rods and cones

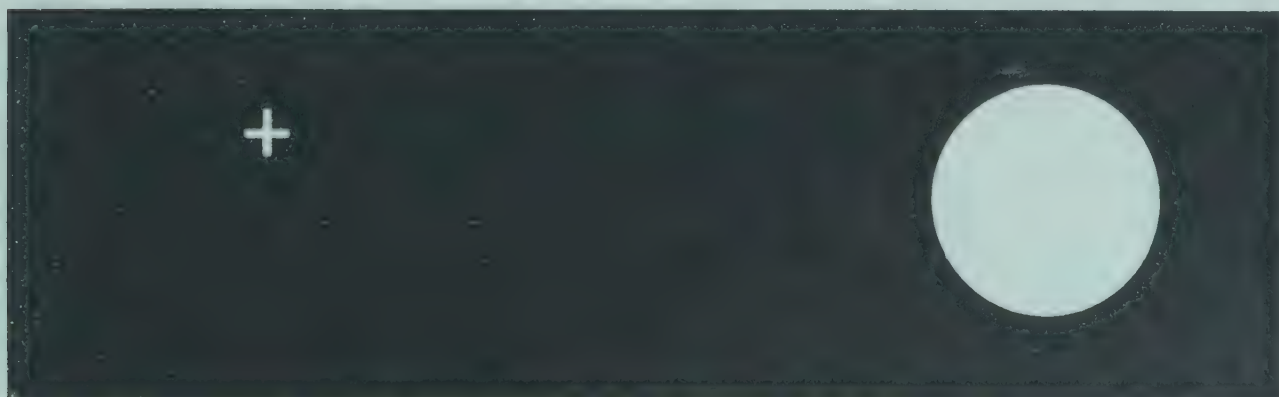
Cones (per square millimetre)	160,000 ⁵
extrafoveal	132,000 ⁴
macular (avascular area)	8000–13,000 ⁶
in the fovea	4000 ²
Total number of cones ⁷	ca. 7 million
Total number of rods ⁷	ca. 130 million

Size of the macula lutea²: 1–3 mm in diameter (corresponding to 4–12°)

Diameter of the fovea centralis² 0.2–0.3 mm

Size of the blind spot² width 5–6°
(point of entry of the optic nerve) height 7–8°

located 12° temporally of and 1.5° below the point of fixation.



Demonstration of the blind spot: With the left eye closed, fix the right eye on the cross: at a distance of ca. 20 cm the white circle disappears.

¹) COUVREUX, C. R. Acad. Sci., 178, 416, 1388, 1924. ²) DUKE-ELDER, W. S., *Textbook of Ophthalmology*, Vol. I, London, 1932. ³) HOTTA, G., *Arch. Ophthalmol.*, 62, 253, 1906. ⁴) EISLER, P., in SCHIECK and BRÜCKNER, *Kurzes Handbuch der Ophthalmologie*, Berlin, 1930–32. ⁵) LAUBER, H., *Handbuch der mikroskopischen Anatomie des Menschen*, Vol. 3, part 2, Berlin, 1936. ⁶) BECKER, O., *Anatomie der gesunden und kranken Linse*, Wiesbaden, 1883. ⁷) GREIFF, R., in *Handbuch der gesamten Augenheilkunde*, Berlin, 1931.

IV. Optic nerve and visual pathway

Optic nerve

Weight ¹ (grams)	right	0.4
	left	0.3
Length (millimetres)		
Total (eyeball–chiasma) ²		35–55
left shorter than right (difference 1–7 mm), shorter in women than in men		
Intraocular portion ³ (depth of the excavation of the optic papilla)		1
Orbital portion ⁴ (eyeball–optic foramen)		
Men (slightly stretched)		24.27
Women (slightly stretched)		23.19
Intraosseous portion ⁵		4–10
Intracranial portion ⁴	right	13
	left	12.8
Diameter (millimetres)		
sheathed portion	without sheath	3 ⁶
	with sheath	4 ⁷
at the entrance into the eyeball		1.5 ⁶ 2 ⁷
Nerve fibre bundles (3 mm average dia.) ⁸		400,000 –500,000
Nerve fibres per bundle		40,000 ⁹ –50,000 ⁶

Visual pathway

Symptoms of conductive disturbances in the visual pathway (numbers refer to the adjacent diagram)

- (1) *Lesion of the optic nerve*: Amaurotic pupillary paralysis: pupil on the blind side slightly larger; direct reaction to light absent, indirect reaction intact. Unaffected eye: direct reaction to light intact, indirect reaction absent. Accomodation to near vision unaffected.
- (2) *Lesion of the chiasma*: Hemianopic paralysis with bi-temporal hemianopia and optic atrophy. On illumination of the nasal halves of the retinae, no direct or indirect reaction on either side; on illumination of the temporal halves of the retinae, prompt direct and indirect reactions. Accomodation to near vision unaffected.
- (3) *Lesion of the right optic tract*: Hemianopic pupillary paralysis on the left side with homonymous hemianopia on the left side and bilateral optic atrophy. Absence of the direct and indirect reactions to light when both retinae are illuminated from the left. Direct and indirect reactions to light intact on illumination from the right.
- (4) *Lesion of the internal capsule or of the optic radiation on the right side*: Homonymous hemianopia on the left side without hemianopic pupillary paralysis.
- (5a),(5b),(5c) *Lesions of the sphincter nucleus or of the sphincter path on the right side*: Absolute pupillary paralysis. In addition to failure of the direct and indirect reactions to light, absence of the convergence reaction on the right side. In the left eye neither the direct and indirect reactions to light nor the convergence reaction are affected.
- (6) *Lesion of the connector neurone system on the right side* between the sensory and motor parts of the reflex arc: Reflex pupillary paralysis (ARGYLL-ROBERTSON pupil). Absence of the direct and indirect reactions to light on the right side, convergence reaction intact with miosis (due to stimulation of the nuclear area by the lesion). All reactions on the left side intact.

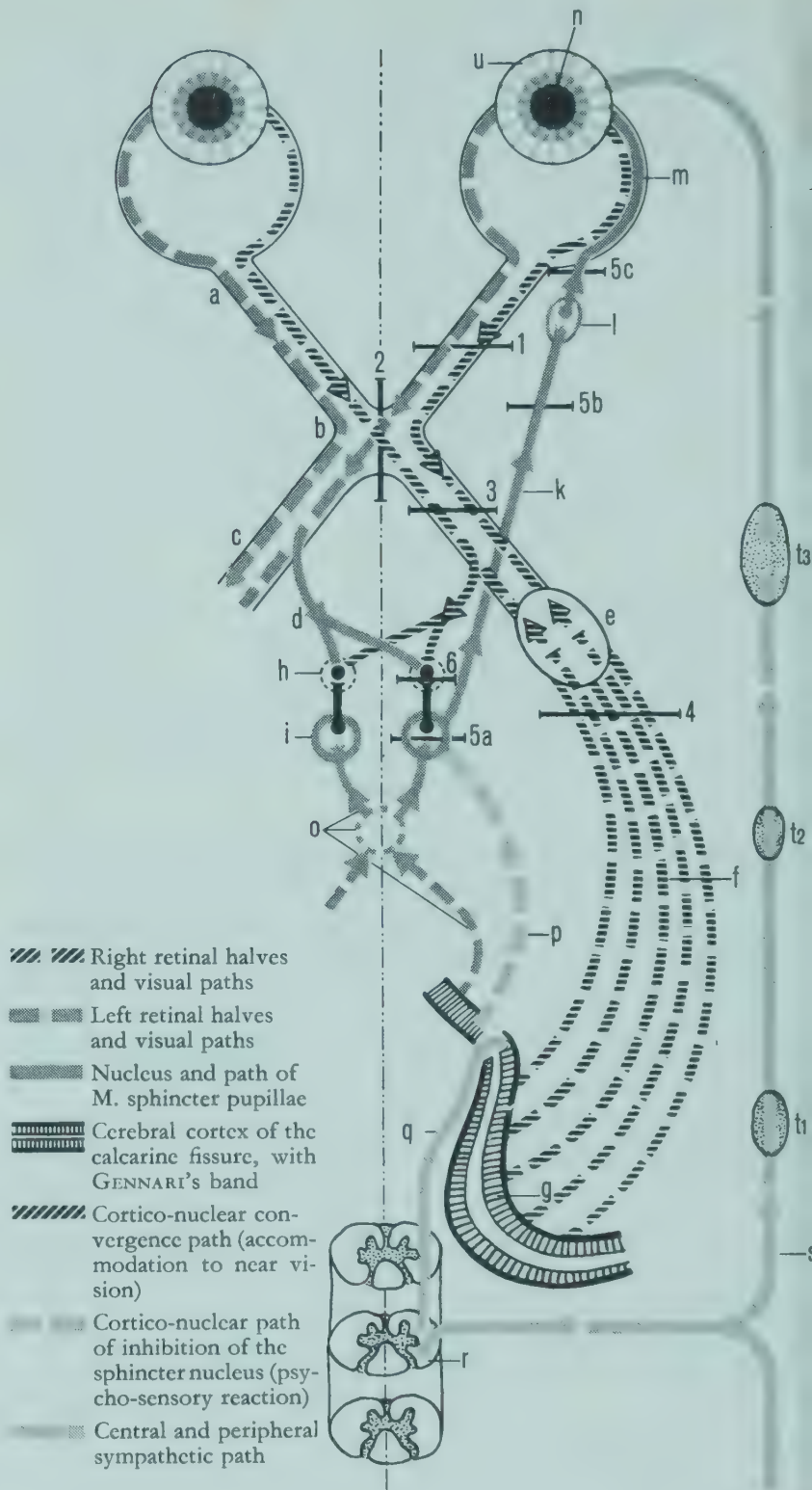


Diagram of the visual and pupillary reflex pathways (after C. BEHR¹⁰)

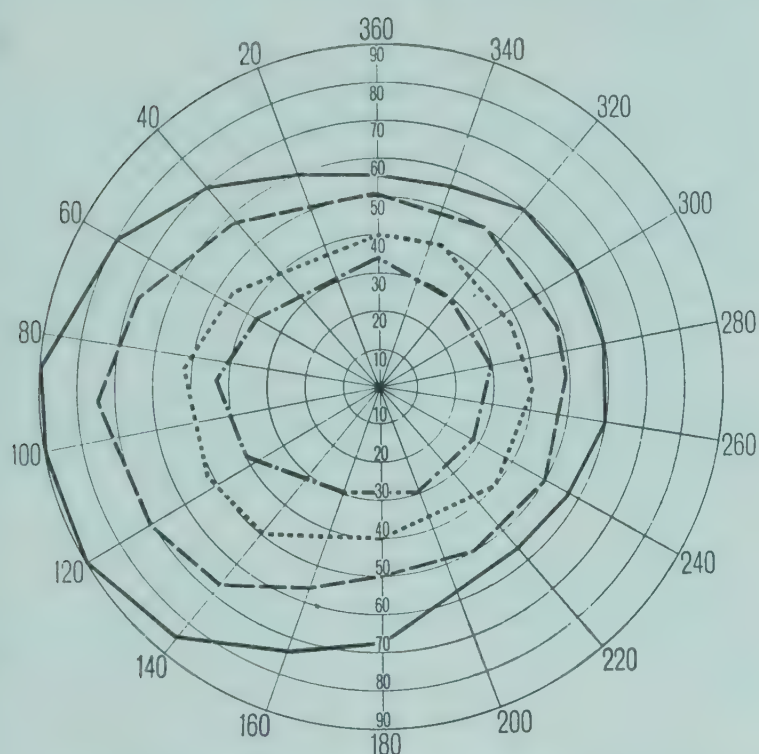
a Optic nerve; b Chiasma; c Optic nerve tract; d Ascending pupillomotor path in the anterior arm of the lamina quadrigemina after its separation from the visual paths; e Lateral geniculate body; f Internal capsule and optic radiation; g Visual perception centre in the cortex of the calcarine fissure; h Connecting neurone system between the ascending pupillary path and i Sphincter nucleus (EDINGER-WESTPHAL nucleus); k Sphincter path in the oculomotor nerve; l Ciliary ganglion; m Intraocular sphincter path (posterior ciliary nerves between choroid and sclera; n M. sphincter pupillae; o Path and subcortical centre of accommodation reaction to near vision (convergence reaction); p Cortico-nuclear inhibition path of the sphincter nucleus; q Central sympathetic path; r Cilio-spinal centre (BUDGE); s Sympathetic trunk; t₁, t₂, t₃ Inferior, median and superior cervical ganglia; u M. dilator pupillae.

¹) VIERORDT, *Anat. usw., Daten und Tabellen*, 3rd ed., Jena, 1906. ²) SCHAEFFER, *Anat. Rec.*, **28**, 243, 1924. ³) HOTTA, G., *Arch. Ophthal.*, **62**, 253, 1906. ⁴) WEISS, *Beitr. Anat. Orbita*, **1**, 50, 1888. ⁵) DUKE-ELDER, W. S., *Textbook of Ophthalmology*, Vol. I, London, 1932. ⁶) GREEFF, R., in *Handbuch der gesamten Augenheilkunde*, Berlin, 1931. ⁷) KUHN, H., *Arch. Ophthal.*, **25**, 179, 1879. ⁸) STEINDORFF, K., *Tab. biol. (Amst.)*, **22** (1), 285, 1947. ⁹) KUHN, H., *Ber. dtsch. ophthal. Ges.*, **90**, 1881. ¹⁰) BEHR, C., in SCHIECK and BRÜCKNER, *Kurzes Handbuch der Ophthalmologie*, Berlin, 1930–32.

The visual field

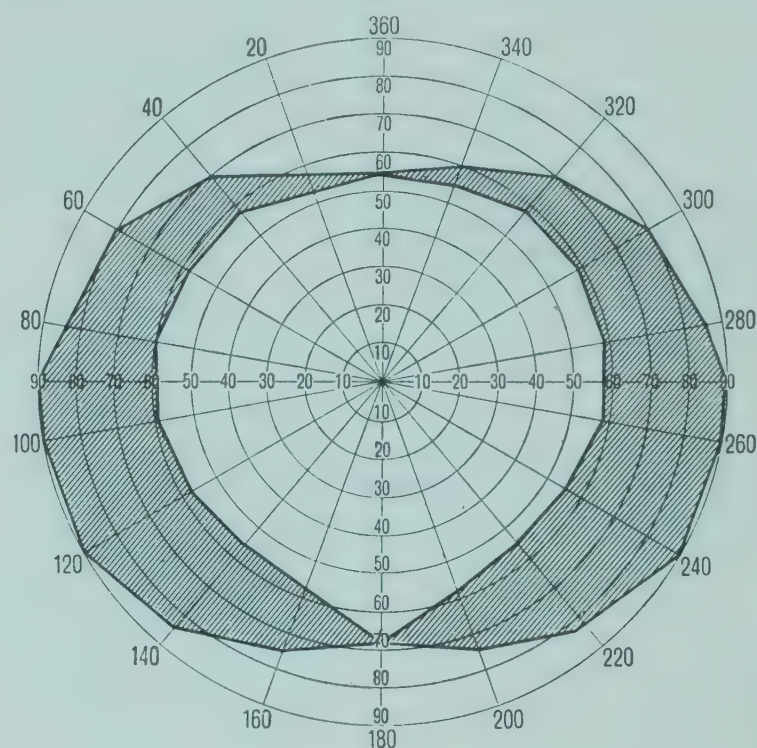
Methods of examination: BJERRUM-screen, MAGGIORE-perimeter, GOLDMANN-perimeter, AMSLER-LANDOLT-screen, etc.

(Bibliography: DUBOIS-POULSEN, *Le champ visuel*, Paris, 1952; H. LAUBER, *Das Gesichtsfeld*, Munich, 1944; TRAQUAIR, *Clinical Perimetry*, 6th. ed., London and St. Louis, 1949.)



Normal visual field of the left eye for white light and colours

— = white field = red field
 - - - - - = blue field - . - . - . = green field



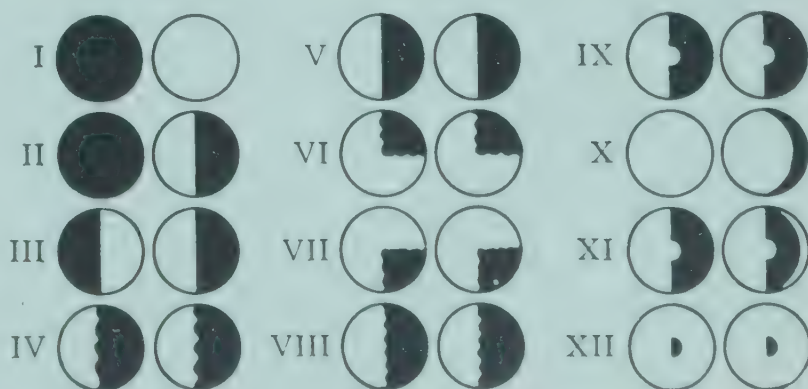
Normal binocular visual field for white light

(Area inside shaded area = overlapping of the right and left fields)
 (after SCHIECK and BRÜCKNER, *Kurzes Handbuch der Ophthalmologie*, Berlin, 1930-32)

Synopsis of the most important visual-field defects

(from DUKE-ELDER, W. S., *Textbook of Ophthalmology*, Vol. IV, London, 1949)

- I = Lesion of the optic nerve – ipsilateral blindness
- II = Lesion of the optic nerve near the chiasma – ipsilateral blindness with contralateral temporal hemianopia
- III = Lesion of the median chiasma – bitemporal hemianopia
- IV = Lesion of the optic tract – markedly incongruous homonymous hemianopia
- V = Lesion at commencement of optic tract, external geniculate body or lower part of radiations – clear-cut homonymous hemianopia without macular sparing
- VI = Lesion of the anterior loop of the optic radiations – markedly incongruous superior quadrantanopia
- VII = Lesion of the inner part of the optic radiations – slightly incongruous inferior quadrantanopia
- VIII = Lesion at the middle of the optic radiations – slightly incongruous homonymous hemianopia without macular sparing
- IX = Lesion of the posterior part of the optic radiations – congruous homonymous hemianopia with macular sparing
- X = Lesion of the anterior part of the calcarine cortex – contralateral blindness in temporal crescent
- XI = Lesion of the middle part of the calcarine cortex – congruous homonymous hemianopia with macular sparing and contralateral sparing of temporal crescent
- XII = Lesion in the region of the occipital pole – congruous homonymous hemianopic central scotoma



Physical and chemical data

(other than those given in the foregoing text)

A. Eyeball as a whole: intraocular pressure¹

	Mean*	Normal Range* (Mean ± 2 σ)	Standard deviation* σ
Normal values ² (mm Hg)	24	18–29	3

Comparison of values obtained with various tonometers³

(Mean values from numerous measurements on normal human eyes) (mm Hg):

Tonometer of		
SCHIÖTZ	BAILLIART	McLEAN
24.21	17.84	35.33

Comparison of values obtained with various tonometers and manometers⁴ (mm Hg):

The pressure differences given by the SCHIÖTZ tonometer do not exceed 1 mm Hg (rabbits), pressure values obtained with the BAILLIART tonometer are smaller, and values obtained with the McLEAN tonometer are greater than manometer values.

Remarks

There is no significant difference between the intraocular pressures of the left and right eyes¹, no significant dependence of the intraocular pressure on physical constitution⁵, left- or right-handedness⁶, sleep^{7, 8}, body temperature⁹, atmospheric pressure¹⁰, pupillary size¹, the accommodation¹¹, blood pressure^{12–15}, or intracranial pressure^{15a}. There is slight variation with the daily rhythm (in adults generally 4–5 mm Hg higher in the morning than in the evening¹⁶, maximum daily variation 6–8 mm Hg¹⁷, increased by emotional disturbances¹⁸, and with the position of the head^{18a} (lowering the head 30° below the horizontal and bending it back^{18b} both increase the intraocular pressure by several mm Hg, raising the head 30° above the horizontal reduces the pressure^{18a}). Significant variations of the intraocular pressure: decreases on ingestion of food¹⁹, varies with the pulse (2–10 mm Hg)²⁰, increases when the neck is compressed (17–46 mm Hg on compression for one minute, similar values for 5 minutes)^{21, 22}.

* The limits of the normal range are strictly defined by the formula: mean value ± 2 × the standard deviation σ (cf. page 32).

B. Lacrimal Secretion

Physical data

Quantity ²³ (grams per hour)	0.03 – 0.05
Osmotic pressure ²⁴	6.9 atm
Freezing-point depression ²⁵	0.551°C
Hydrogen-ion concentration	
pure ²⁶	pH 7.53 – 7.95
with conjunctival secretion ²⁶	pH 7.98 – 8.29
pure ²⁷	pH 7.35
with conjunctival secretion ²⁸	pH 7.23 ± 0.13
with conjunctival secretion and increased lacrimal secretion ²⁸	pH 7.44 ± 0.21

Chemical composition²⁵ (in mg/100 ml)

Dry substance	1800
Ash	1050
Total protein	669
Albumins	394
Globulins	275
Total nitrogen	158
Non-protein nitrogen	51
Urea	30
Ammonia (NH ₄)	5
Glucose	65
Chloride, as Cl	394
Chloride, as NaCl	658
Sodium, Na	445
Potassium, K	116

Human lacrimal secretion contains specific immune bodies²⁹ and the enzyme lysozyme, which has also been found in the lacrimal secretion of animals⁴².

C. Anterior eye chamber (Camera anterior)

Volume ³⁰ (per cent of the eyeball volume)	4
Depth	

Depth as a function of age ³¹			
Age (years)	Emmetropia	Depth (millimetres) Hypermetropia	Myopia
0–20	3.69	3.37	3.83
21–50	3.57–3.42	3.28	3.85
41–60	3.27–3.15	2.99	3.66
over 60	3.04	3.03	3.66

Depth as a function of accommodation ³²		
Accommodation (diopters)	Depth (millimetres) apparent	actual
1 (relaxation)	3.68	3.33
4	3.55	3.22
6	3.50	3.17
9	3.34	3.06

Aqueous humour

Physical data

	Mean	Range
Quantity	0.223 ³³	0.15–0.35 ³⁴
Specific gravity ³⁵		1.002–1.009
Osmotic pressure ³⁶	7.10 atm	
Freezing point depression ³⁷	0.568°C	
Viscosity ³⁸ (H ₂ O = 1)		1.024–1.040
Surface tension ³⁹ (at 37°C, dyn cm ⁻¹)	60.4	
Index of refraction ³⁸ (PULFRICH refractometer)		1.33366–1.33700
Specific conductivity ³⁹ (at 37°C, Ω ⁻¹ cm ⁻¹)	0.0173	
Hydrogen-ion concentration		
Quinhydrone electrode ⁴⁰	pH 7.27	7.16–7.76
Electrometric ⁴¹		pH 7.15–7.23

¹) ASCHER, K. W., *Tab. biol. (Amst.)*, **22** (1), 331, 1947. ²) MÜLLER, H. K., *Arch. Augenheilk.*, **104**, 89, 1931. ³) SHOJI, *Acta Soc. ophthalm. jap.*, **35**, 371, 1931. ⁴) SUZUKI, S., *ibid.*, **39**, 1277, 1935. ⁵) GENNARO, *7. Congr. Soc. ital. Ottal. Roma*, 1931, ref. *Zbl. Ophthalm.*, **28**, 633, 1933. ⁶) MARX, E., *Ned. T. Geneesk.*, **2**, 1082, 1923. ⁷) RYCROFT, B., *Trans. ophthalm. Soc. U. K.*, **55**, 333, 1933. ⁸) POOS, F., *Klin. Mbl. Augenheilk.*, **94**, 163, 1935. ⁹) DE DECKER, J. F., *Arch. Augenheilk.*, **100**, 101, 180, 1929. ¹⁰) ASCHER, K. W., *Klin. Mbl. Augenheilk.*, **69**, 525, 1922. ¹¹) TESSIER, G., *Ann. Ottal.*, **57**, 799, 1929. ¹²) BRUNS, Chr., *Klin. Mbl. Augenheilk.*, **71**, 90, 1923. ¹³) BLOCK, *Arch. Neurol. Psychiat.*, **11**, 444, 1924. ¹⁴) WESSLEY, K., *Arch. Augenheilk.*, **78**, 248, 1915. ¹⁵) FOURRIÈRE, *Ann. Oculist.*, **149**, 26, 1913. ^{15a}) CASOLINO, *Ann. Ottal.*, **43**, 554, 1914; MERKULOW, I., *Trans-Ukrain. Hirshman mem. Ophthalm. Inst.*, **3**, 20, 1935, ref. *Zbl. Ophthalm.*, **38**, 209, 1937; ASCHER, K.W., sec¹. ¹⁶) MAGITOT, A., *J. Physiol. Path. gén.*, **21**, 44, 1923. ¹⁷) COLOMBO, L., *Boll. Oculist.*, **2**, 229, 1924. ¹⁸) KAWABATA, H., *Chuo-Ganka-Ibo*, **26**, 4, 1934, ref. *Zbl. Ophthalm.*, **31**, 719, 1934. ^{18a}) WEGNER, W. Z., *Augenheilk.*, **55**, 381, 1925. ^{18b}) TESSIER, G., *Lett. oftal.*, **7**, 311, 1930, ref. *Zbl. Ophthalm.*, **24**, 83, 1931. ¹⁹) PISSARELLO, C., *Ann. Ottal.*, **44**, 1915, ref. *Klin. Mbl. Augenheilk.*, **59**, 687, 1917. ²⁰) BAILLIART, P., *Bull. Soc. franç. Ophthalm.*, **48**, 294, 1935. ²¹) HIROSE, S., *Acta Soc. ophthalm. jap.*, **36**, 1184, 1932. ²²) SCHULZE, E., *Z. Augenheilk.*, **17**, 222, 1907. ²³) SCHIRMER, O., *Arch. Ophthalm.*, **56**, 197, 1903. ²⁴) Calculated from ²⁵. ²⁵) RIDLEY, F., *Trans. ophthalm. Soc. U. K.*, **50**, 268, 1930. ²⁶) GARDILËT, A., *Arch. Ophthalm.*, **137**, 71, 1937. ²⁷) HOSFORD and HICKS, *Arch. Ophthalm.*, **13**, 14, 1935. ²⁸) SWAN et al., *Proc. Soc. exp. Biol.*, **42**, 296, 1939. ²⁹) FLEMING and ALLISON, *Brit. J. exp. Path.*, **6**, 87, 1925. ³⁰) MAGITOT, A., *Ann. Physiol. Physicochim. biol.*, **2**, 363, 1926. ³¹) RAEDER, *Arch. Ophthalm.*, **110**, 73, 1922. ³²) FINCHAM, *Trans. ophthalm. Soc. U. K.*, **26**, 239, 1924–25. ³³) Calculated from the mean values given by the following authors: EMMERT, *Z. vgl. Augenheilk.*, **4**, 40, 1886; MAGITOT, A., *Ann. Physiol. Physicochim. biol.*, **2**, 363, 1926; NIELSNAFF, E., *Arch. Ophthalm.*, **42**, 4, 1, 1896; O'BRIEN, C. S., *C. R. 8^e congr. ophthalm.*, 1929, **1**, 150, 1930. ³⁴) Lowest and highest mean values from ³², ³⁵) STJNDORFF, *Handbuch der Biochemie*, 1908, quoted by DUKE-ELDER³⁸. ³⁶) Calculated from ³⁷, ³⁷) DILLER, *Arch. Augenheilk.*, **96**, 179, 1935. ³⁸) DUKE-ELDER, W. S., *Textbook of Ophthalmology*, London, Vol. I, 1932. ³⁹) MAGITOT, A., *Ann. Physiol. Physicochim. biol.*, **2**, 363, 1926. ⁴⁰) BAURMANN, M., *Arch. Ophthalm.*, **118**, 369, 1927. ⁴¹) KUBIK, J., *Arch. Augenheilk.*, **98**, 483, 1928. ⁴²) SCHUHMACHER, H., *Z. Immunforsch.*, **110**, 389, 1953.

Remarks on the chemistry of the aqueous humour, lens and vitreous body: Owing to the paucity of material for examination the literature contains only sparse and incomplete data on the chemical composition of the aqueous humour, lens and vitreous body of the normal human eye. On the other hand, human cataract lenses as well as the aqueous humour, lens and vitreous body of animals, particularly of the horse and cattle, have been

thoroughly investigated (see SÜLLMANN¹). However, pathological changes or species differences render such data of little clinical value and they have therefore been omitted from these *Tables*, the object of which is to provide a summary of normal values for man. An exception has been made in the case of the protein fractions of the lens and vitreous body in order to emphasize the difference between these and the blood-protein fractions.

Aqueous humour (continued)

Chemical composition (values in mg/100 ml)

Dry substance ¹	approx. 1200
Total protein	6 ² –18 ³
200 (50–375) in regenerated aqueous humour, mainly dependent upon the anaesthetic used (lowest values with cocaine). Greatly increased in iridocyclitis (up to 457), glaucoma, congenital hydrophthalmia ⁴ .	
Albumin-globulin ratio ²	1
Urea	12.94–30 ⁵
Amino-acids (as glycine) ⁶	25–220
Uric acid ⁴	2.8 (1.1–4.5)
Reducing substances (glucose) ⁷	70–160
Mean 100	
Hexosamine ⁸	14.9–18.3
Mean 16.0	
Lactic acid ⁹	20.5–24
Citric acid ¹⁰	1.6–3.2
Ascorbic acid ¹¹	5–29.5
Mean 15.5	
Inorganic constituents	
Phosphorus (inorganic) ⁴	1.7–2.1
Mean 1.92	
Chloride (as Cl) ¹²	357–465
Mean 427	
Carbon dioxide (vol%) ¹³ , normal	61.0–74.2
in inflammatory conditions	65.2–80.4

D. Lens

Physical data

Thickness ¹⁴ (millimetres)	0–20 years	3.92
	21–40 years	4.05
	41–60 years	4.80
	over 60 years	4.84

Diameter (equator) (millimetres)

Children		Adults ¹⁸	
Newborn ¹⁵	6.77	20–29 years	8.67
4 months ¹⁶	3.3	30–39 years	8.96
5 months ¹⁶	4.0	40–49 years	9.09
7 months ¹⁶	5.0	over 50 years:	over 9.4
9–12 months ¹⁷	7.46		
12 years ¹⁷	8.8		

Surface ¹⁹ (sq. millimetres)	Adults	approx. 250
	Newborn	approx. 143

Weight (milligrams), volume (cubic millimetres) and specific gravity

Children ²⁰	Weight	Adults ¹⁸	Weight	Volume	Specific gravity
Newborn	65.6	20–29 years	174	163	1.067
1– 3 months	92.8	30–39 years	192	177	1.085
4– 5 months	100.9	40–49 years	204	188	1.085
10–11 months	124.5	50–59 years	221	205	1.078
1–10 years	146.8	60–69 years	240	225	1.067
10–20 years	152.8	over 70 years	over 240	over 227	—

Lens (continued)

Physical data (continued)

Index of refraction ^{21a} :	Anterior cortex ...	1.387
	Posterior cortex ..	1.385
	Nucleus	1.406
Osmotic pressure ²¹		7.23 atm
Freezing-point depression ²²		0.58° C
Hydrogen-ion concentration ²³		pH 7.5

Chemical composition

(values in mg/100 g, unless otherwise stated)

Dry substance ²⁴ (grams/100 grams)	30
no significant change with age (slight increase) ²⁵ , no significant difference between normal and cataract lenses ²⁵	
Ash ²⁶	1040
Total protein ²⁷ (per cent of dry substance) .	94.7
Protein fractions (<i>cattle</i>) ²⁹ (per cent of total protein)	
Albuminoid substances (insol. in water) .	12.5
α crystallins	31.74
β crystallins	} extractable with water ...
Albumin	
Mucoproteins	1.46
Nucleoproteins	0.84
Non-protein nitrogen ²⁹	0.07
	40.5–84.5
	Mean 57.3
Reducing substances (glucose) ³⁰	46–88
	Mean 60

Lipids³¹ (per cent of dry substance)

Age (years)	Total lipids	Phospho-lipids	Total cholesterol	Free cholesterol
0– 1	2.12	0.41	1.71	—
1–10	6.14	3.13	0.83	0.49
10–20	8.28	4.77	0.52	0.32
20–30	—	4.13	0.74	0.64
30–50	—	3.60	0.89	0.59
60–70	6.48	3.04	1.06	0.43
70–75	8.35	4.43	1.30	0.74

Ascorbic acid ³²	17.8–42.5
	Mean 30.0

Inorganic constituents

Phosphate (ortho-, as PO ₄) ²⁶	193
Sulphate (as SO ₄) ²⁶	486
Chloride (as Cl) ²⁶	35.3
Sodium, Na ²⁶	131
Potassium, K ²⁶	227
Calcium, Ca ²⁶	10.5
Magnesium, Mg ³³ (mg per lens)	0.014
Silicon, Si ³⁴	none
Copper, Cu ³⁵	0.4
Zinc, Zn ³⁶	0.95–1.18

¹ SÜLLMANN, H., *Chemie des Auges*, in *Tab. biol. (Amst.)*, 22 (2), 1, 1951; FISCHER, F. P., *Physikalische Chemie des Auges*, *ibid.*; MARQUARD, P., with addendum SÜLLMANN, H., *Fermente des Auges*, *ibid.*; BUSCHKE, W., *Vitamine und verwandte Stoffe des Auges*, *ibid.*; KRAUSE, A. C., *Sehpurpur*, *ibid.* ² KRONFELD, P. C., *Amer. J. Ophthal.*, 24, 1121, 1941. ³ KRONFELD et al., *ibid.*, 24, 264, 1941. ⁴ WALKER, A. M., *J. biol. Chem.*, 101, 269, 1933. ⁵ MOORE et al., *Arch. Ophthal.*, 27, 317, 1942. ⁶ RADOS, A., *Arch. Ophthal.*, 109, 342, 1922. ⁷ ASK, F., *Klin. Mbl. Augenheilk.*, 78, Suppl. 33, 1927. ⁸ PALMER et al., *J. biol. Chem.*, 119, 491, 1937. ⁹ NONAKA, M., *Acta Soc. ophthal. jap.*, 35, 110, 1931. ¹⁰ GRÖNVALL, H., *Acta ophthal.*, Suppl. 14, 1937. ¹¹ Calculated from the values given by MÜLLER and BUSCHKE, *Arch. Augenheilk.*, 108, 368, 1934; BIETTI, G., *Boll. Oculist.*, 14, 3, 938, 1935; FRANTA, J., *Arch. Augenheilk.*, 110, 574, 1937; VLADESCO and STEFANO, *C. R. Soc. Biol.*, 132, 169, 1939. ¹² GALA, A., *Bratislavské lekár. Listy*, 3, 192, 1924. ¹³ KRONFELD, P. C., *Arch. Ophthal.*, 118, 606, 1927. ¹⁴ RAEDER, *Arch. Ophthal.*, 110, 73, 1922. ¹⁵ v. PFLUGK, *Klin. Mbl. Augenheilk.*, 47, 1, 1909. ¹⁶ COLLINS, R., *London Ophthal. Hosp. Ref.*, 13, 1890, quoted by STEINDORFF, K., *Tab. biol. (Amst.)*, 22 (1), 166, 1947. ¹⁷ DUB, *Arch. Ophthal.*, 37, 426, 1891. ¹⁸ PRIESTLEY-SMITH, *Trans. ophthal. Soc. U. K.*, 3, 79, 1883. ¹⁹ HESS, C., in *Handbuch der gesamten Augenheilkunde*, 2nd ed., Leipzig, 1905. ²⁰ KNORR, *Würzburger Abhandlungen*, 5, 4, 1929. ²¹ Calculated from ²². ^{21a} FREYTAG, quoted by DUKE-ELDER, *Textbook of Ophthalmology*, London, Vol. I, 1932. ²² NORDMANN, J., *Arch. Ophthal.*, 52, 78, 1935. ²³ LABBÉ and LAVAGNA, *Clin. ophthal.*, 15, 131, 1926. ²⁴ DEUTSCHMANN, R., *Arch. Ophthal.*, 25, 213, 1879. ²⁵ SALIT, R. W., *Amer. J. Ophthal.*, 21, 755, 1938. ²⁶ MACKAY et al., *Brit. J. Ophthal.*, 16, 193, 1932. ²⁷ CAHN, A., *Hoppe-Seyl. Z. physiol. Chem.*, 5, 213, 1881. ²⁸ KRAUSE, A. C., *Arch. Ophthal.*, 10, 788, 1933. ²⁹ DE VECCHI, J., *Boll. Oculist.*, 16, 400, 1937. ³⁰ LOTTRUP-ANDERSEN, CHR., *Acta ophthal.*, 5, 226, 1927. ³¹ GOLDSCHMIDT, M., *Biochem. Z.*, 127, 210, 1922. ³² HAWLEY and PEARSON, *Arch. Ophthal.*, 19, 959, 1938. ³³ GIVNER and GANNON, *ibid.*, 19, 941, 1938. ³⁴ EVANS and KERN, *J. Ophthal.*, 14, 1029, 1931. ³⁵ BEZSSONNOFF and LEROUX, *C. R. Soc. Biol.*, 140, 605, 1946. ³⁶ LEINER and LEINER, *Biol. Zbl.*, 62, 119, 1942.

Cover test: With one eye covered the patient fixes his regard on the examiner's finger. If the covered eye possesses a latent strabismic tendency it will then assume a convergent or divergent strabismic position since it is no longer stimulated to binocular vision. This becomes apparent when the cover is transferred to the other eye: the strabismic eye immediately jumps from its position back into the line of fixation. Latent divergent strabismus is known as *exophoria*, latent convergent strabismus as *esophoria*, latent upward deviation as *hyperphoria*, and latent downward deviation as *hypophoria*.

MADDOX test: The patient fixes his regard on a point source of light. A specially constructed prism (MADDOX prism), which refracts the point to a vertical luminous line, is placed before the left eye. If the ocular muscles are properly balanced this vertical line, as seen by the left eye, coincides with the point of light seen by the right eye. If there is a latent disturbance of the dynamic balance of the ocular muscles the line and the point are no longer seen as coincidental. The greater the apparent distance between the line and the point, the greater the degree of heterophoria: in exophoria the line is seen to the right of the point (crossed diplopia), in esophoria to the left of the point (uncrossed diplopia).

Ocular symptoms due to brain tumours¹

I. General symptoms (intracranial pressure)

- | | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>1. Papillary oedema normal vision long retained, normal peripheral visual field, enlarged blind spot.</p> <p>Differential diagnosis:</p> <p><i>Optic neuritis</i> rapid impairment of vision, central scotoma, peripheral defects in visual field.</p> <p><i>Optic papillitis</i></p> <p><i>Malignant hypertensive retinopathy</i> extensive vascular changes, centres of fatty degeneration, retinal exudation centres.</p> <p>Differential diagnosis of commencement of papillary oedema:</p> <p><i>Pseudoneuritis</i> with or without tortuositas vasorum, frequent in hypermetropia, skull deformities.</p> <p><i>Papillary nodules</i> particularly hidden ones (note hereditary character).</p> | <p><i>Chronic-atrophic papillary oedema</i> loss of central visual clarity up to amaurosis, concentric restriction of the peripheral field.</p> <p>2. Abducens pareses uni- or bi-lateral, topically not utilizable.</p> <p>3. Clivus border syndrome, consisting of:</p> <p>unilateral <i>mydriasis and pupillary paralysis, ptosis</i>;
in late stages, oculomotor/ocular-muscle pareses with unconsciousness.</p> <p><i>Aetiology</i>: Compression of the oculomotor nerve immediately behind its exit from the base of the brain, either on one side of the clivus border of the tentorial aperture or on the transverse superior cerebellar artery.</p> |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

II. Local symptoms

1. Tumours of the frontal lobe

FOSTER KENNEDY syndrome (unilateral primary optic atrophy on the tumour side, papillary oedema on the opposite side), rare.

Bitemporal and homonymous defects; tubular visual fields in cases of severe stimulation weakness.

2. Tumours of the temporal lobe

Formed, differentiated visual hallucinations, alone or combined with hallucinations of taste and smell (uncinate fits).

Typical: homonymous hemianopia in the upper quadrants or sectors (MEYER's loop).

In addition, lower quadrantopias and total homonymous hemianopias.

Homolateral mydriasis and pupillary paralysis (clivus border syndrome).

Homolateral oculomotor and central facial paresis.

3. Tumours of the parietal lobe

Alexia (word-blindness), visual agnosia (psychic blindness).

Lower homonymous quadrantopia, total homonymous hemianopia when lesion extends occipitally.

4. Tumours of the occipital lobe

Subjective loss of vision on one side, optical hallucinations of a formless nature (light flashes, discs, blinking lights, etc.), occasionally micropsia.

Total homonymous hemianopia with or without sparing of the macula: congruence of the defects and of the residual visual fields.

Frequently papillary oedema with multiple haemorrhages and exudatory points.

Horizontal nystagmus (cerebellar compression).

5. Pituitary tumours (only the chromophobic and eosinophilic adenomas are of ophthalmoneurological importance)

Chiasmal syndrome:

Subjective: impairment of vision, often unilateral, later bilateral, haziness or foggiess of vision, visual field defects, "horse-blinkers". The chronic head and eye pains often cease concurrently with the onset of visual defects.

Objective: classically, *bitemporal hemianopia*, beginning in the upper temporal quadrants, extending to the lower temporal and later the lower nasal and finally to the upper nasal quadrants.

(continued on the next page)

¹) After HUBER, E., *Augensymptome bei Hirntumoren*, Berne, 1956.

Pituitary tumours (continued)

Typical: symmetry of the visual field defects, also the chronological development.

Relatively frequent central or paracentral *scotoma*.

Non-typical: amaurosis of the one eye with temporal hemianopia of the other.

Fundus of the eye: primary simple *optic atrophy*, uni- or bi-lateral.

Possible ocular-muscle paresis (III, VI) if extrasellar expansion occurs, and even cavernous sinus syndrome (III, IV, V, VI).

Radiography: balloon-shaped enlargement of the sella, thinning of the sellar floor, which extends into the sphenoidal sinus, erosion of the clinoid processes.

6. Craniopharyngioma – intra- and extra-sellar tumour type

In children, early increase in intracranial pressure and therefore frequent bilateral papillary oedema.

In adults, optic atrophy with lateral variations.

Bitemporal hemianopia with asymmetric character and development of the defects.

Subjectively, often sudden worsening or improvement of vision (cystic nature of the tumour): note possible *confusion with retrobulbar neuritis*.

Radiography: suprasellar calcification, massive or in the form of irregular spots.

7. Glioma of the optic chiasma

Mostly in children, usually a sign of generalized neurofibromatosis, asymmetric chiasmal syndrome.

Radiography: gourd- or omega-shaped sella, uni- or bi-lateral enlargement of the optic foramen.

8. Meningeoma of the tuberculum sellae – suprasellar tumour type

Subjective impairment of vision at first in *one* eye.

In early stages frequent unilateral central scotomas: note possible *confusion with retrobulbar neuritis*.

Later amaurosis of one eye with temporal hemianopia of the other. In addition, bitemporal hemianopia mostly with distinctly asymmetric character and development.

Optic atrophy, unilateral, or unilaterally more severe.

Radiography: hyperostosis of the tuberculum sellae.

9. Olfactory meningeoma

Subjectively, mainly uni- or bi-lateral *anosmia*.

As a result of compression of the basal frontal lobe, *organic psychosyndrome* to a greater or lesser degree.

Objective ophthalmological signs, not specially characteristic: scotoma, nasal visual field defects, more or less typical bitemporal hemianopias, amaurosis of one eye and temporal hemianopia of the other.

Fundus: unilateral optic atrophy, more frequently bilateral papillary oedema (especially in cases of bilateral anterior meningeoma).

FOSTER KENNEDY syndrome *very rare*.

Radiography: hyperostosis in the area of the olfactory groove or above the tuberculum sellae.

10. Sphenoid wing meningeoma – parasellar tumour type

Subjective: diplopia, impairment of vision in one eye, with protrusion of this eye.

Objective: unilateral *exophthalmus*

ocular-muscle pareses (VI, III frequent), possibly even cavernous sinus syndrome with III, IV, V (weakening of the *corneal reflex*) and VI affected.

Initially unilateral (predominantly nasal) visual field defects, later *homonymous hemianopia* (optic tract or temporal lobe).

Fundus: unilateral optic atrophy, bilateral papillary oedema when the tumour is large.

FOSTER KENNEDY syndrome relatively frequent, rare however in the fully developed classical case.

Radiography: thickening and induration of the sphenoid wing and the surrounding areas of the superior orbital fissure.

11. Tumours of the third ventricle

Early circulatory disturbances of the cerebrospinal fluid and development of internal hydrocephalus with *papillary oedema* (often chronic with secondary atrophy). Pressure of the dilated ventricle on the chiasma can lead to asymmetric chiasmal syndromes with primary optic atrophy.

12. Tumours of the midbrain and epiphysis (pinealoma)

PARINAUD syndrome: paralysis of upward movement of the eye, pupillary disturbances of ARGYLL-ROBERTSON type, nuclear trochlear and oculomotor/ocular-muscle pareses; less frequently convergence paralysis or convergence spasms as well as retractor nystagmus.

13. Cerebellar tumours

Early appearance of papillary oedemas, rapidly developing into atrophy.

Principal ocular symptom: horizontal nystagmus, usually more pronounced on the tumour side than on the other. With tumours of the vermis cerebelli, vertical nystagmus also. Non-specific uni- or bi-lateral abducens pareses due to intracranial pressure.

14. Tumours of the fourth ventricle

Early increase of intracranial pressure with papillary oedemas; severe horizontal nystagmus, lateral visual pareses, possibly even convergence spasms.

15. Tumours of the cerebellopontile angle

(prototype: acoustic neurinoma)

Frequent early ocular symptom: homolateral weakening of the corneal reflex (as partial symptom of injury of the trigeminus).

Later, unilateral lagophthalmus as partial symptom of homolateral facial paresis.

Homolateral abducens paresis, developing only later.

Horizontal nystagmus, more severe on the tumour side than on the other.

Papillary oedema also relatively late, without peculiarities typical for this localization.

16. Tumours of the pons and medulla oblongata

Predominantly supranuclear paralysis of horizontal eye movements, frequently combined with horizontal nystagmus (rarely with horizontal-vertical nystagmus). The visual paralysis is frequently associated with unilateral nuclear abducens paresis.

As a result of the frequent trigeminal lesion, absence or weakening of the corneal reflex.

Papillary oedema extremely rare (only when the tumour extends to the fourth ventricle).

Foreword

The table which follows presents a summary of the data on usual and maximal doses for adults, collated from the principal Pharmacopoeias, of the most important drugs in current use. It must be emphasized that the data given are selective and that no claim for completeness is made. A dash (—) indicates that the substance is listed in the Pharmacopoeia concerned but that no dose is given.

The drugs are listed in the alphabetical order of the English forms of their names (usually as given in the BRITISH PHARMACOPOEIA) with the Latin forms (usually as given in the PHARMACOPOEA INTERNATIONALIS) immediately following. In the interests of a wider circle of users, Latin names which differ considerably from the English forms are included in the alphabetical arrangement (e.g. Hydrargyrum, Natrium). Proprietary *brand names* are printed in *italics*.

Unless otherwise stated the doses are given in *grams*. In view of the somewhat different meanings accorded to the expressions "maximal" and "usual", a summary of the definitions given in the various Pharmacopoeias is appended.

PHARMACOPOEA INTERNATIONALIS 1951 and 1955;
- PHARMACOPOEA GALLICA 1949

The *usual doses* correspond to an average posology and are intended to serve only as a general indication. They are difficult to define within narrow limits since they vary according to the therapeutic effect desired, the susceptibility of the patient, the duration of the treatment, etc. *Those doses which are not usually exceeded are preceded in the table by the words "up to"*.

The *maximal doses* are those which are not usually reached because of the danger of poisoning. *They may only be exceeded when special precautions are taken.*

BRITISH PHARMACOPOEIA 1953 and BRITISH
PHARMACEUTICAL CODEX 1954

The *doses* given are not authoritatively binding upon prescribers but are intended for general guidance. They represent, unless otherwise stated, the average range of

quantities which are generally regarded as suitable for oral administration to adults. Many of these doses may be repeated 3–4 times in 24 hours. They do not indicate the maximum amounts which may be given. The prescriber should exercise his own judgment and act on his own responsibility with regard to the amount or frequency of any dose.

UNITED STATES PHARMACOPEIA XV

The *usual doses* are average doses (neither minimum nor maximum) which may reasonably be expected to produce the therapeutic effect for which the drug is usually employed. They are not obligatory on the prescriber and do not forbid him to prescribe larger doses when in his judgment this may seem advisable.

PHARMACOPOEA HELVETICA V

The *maximal doses* are the largest quantities which the apothecary may dispense for administration to adults either singly (*dosis maxima simplex*) or in the course of 24 hours (*dosis maxima pro die*), unless the prescribing physician expressly directs otherwise.

The *maximal doses* are based on clinical experience and are intended only to avoid as far as possible the danger of poisoning arising through inadvertent error. They do not represent limits the overstepping of which will automatically entail poisoning. On the other hand they are not doses necessarily suitable to any manner of administration. The PHARMACOPOEA HELVETICA gives special maximal doses for subcutaneous injection (*doses maximae ad iniectionem hypodermicam*).

DEUTSCHES ARZNEIBUCH 6

The *maximal doses* are the largest quantities which the apothecary may dispense for administration to adults either singly or in the course of 24 hours, unless the prescribing physician expressly directs otherwise. These doses apply practically to any case where resorption of the drug may be expected.

Abbreviations:

alk. alkaloids
B.P. BRITISH PHARMACOPOEIA 1953
B.P.C. BRITISH PHARMACEUTICAL CODEX 1954
c.d. controlling dose
D.A.B. DEUTSCHES ARZNEIBUCH 6
div. divided dose
emet. emetic dose

gtt. drops
i.d. initial dose
i.m. intramuscular
i.v. intravenous
I.U. international units
m.d. maintenance dose
mg milligram

min. minimum
ml millilitre or ccm
o. oral
p.d. per day
P.G. PHARMACOPOEA GALLICA VII
P.H. PHARMACOPOEA HELVETICA V
P.I. PHARMACOPOEA INTERNATIONALIS

r. rectal
s.c. subcutaneous
s.d. single dose
s.l. sublingual
tot. total
U. units
U.S.P. UNITED STATES PHARMACOPEIA XV

	Usual Doses in grams (unless otherwise stated)				Maximal Doses in grams (unless otherwise stated)					
	B.P. or B.P.C.	U.S.P.	P.I., P.G., etc.		P.I.		P.H.		D.A.B.	
	oral unless otherwise stated				oral unless otherwise stated		oral or parenteral unless otherwise stated			
	single	single	single	per day	single	per day	single	per day	per day	
Acetanilide, Antifebrin (Acetanilidum)			0.1	0.3			0.3	1.0	0.5	1.5
Acetarsol (Acetarsolum)	0.06-0.25		0.05	0.05-0.25	1		0.25	1.0		
Acetarsol Sodium (Acetarsolum Solubile)										
Acetophenetidin. See Phenacetin										
Acetyl- <i>p</i> -aminophenyl Salicylate (Acetylparaminosalolum)			0.5-1.5	—			2	6		
Acetylcholine Chloride (Acetylcholinium chloratum)			0.02-0.2 s.c. i.m.	0.05-0.2 s.c.	—		0.6; 0.4 s.c.	1.5		
Acetylsalicylic Acid (Acidum Acetylosalicylicum)	0.3-1	0.6 every 4 hours	0.5	—	1	6	—	—	—	—
Acidum Arsenicosum. See Arsenic Trioxide										
Aconite (min. 0.8% alk.) (Tuber Aconiti)			—	—	—		0.02	0.06		
Aconite, Powdered (0.5% alk.) (Pulvis Aconiti)	—		—	—	—		0.02	0.06		
Aconite Tincture (0.05% alk.) (Tinctura Aconiti)			0.20	0.60	0.40	1	0.3	1		

Aconitine (Aconitium)		0.0001	—	0.0002	0.0005	0.0001	0.0003	
Adonis Tincture . . (1 g = 0.2 g Herba (Tinctura Adonidis) Adonidis)		1	3					
Adonis Vernalis (Herba Adonidis)		2	6					
Adrenaline* (Adrenalinum)	0.0001–0.0005 s.c.	0.0005 o. s.c.	0.0005 every 4 hours; 0.002 i.m. every 8–16 hrs.	0.002; 0.001 s.c.	0.005; 0.002 s.c.	0.001; 0.0005 s.c.	0.004; 0.002 s.c.	
Adrenaline HCl Solution (1 ^o / ₁₀₀) (Solutio Adrenalini HCl)	—					1 ml; 0.5 ml s.c.	4 ml; 2 ml s.c.	
Agaracin (Acidum Agaricinicum)	0.005–0.03	—				0.03	0.1	0.1
Alcohol Trichloroisobutylicus. See Chlorbutol								
Allobarbitone (Allobarbitalum)	0.03–0.2					0.3	0.6	
Aloes	0.12–0.3		0.25			—	—	—
Aloin (Aloinum)	0.015–0.06							
Amidone HCl. See Methadone HCl								
Amidopyrine (Amidopyrinum)	0.3–0.6	0.3		0.5	1.5	0.5	1.5	—
Aminophylline (Aminophyllinum)	0.1–0.5 o. i.m. i.v.	0.1–0.5 o. i.m. i.v.	0.2 3×p.d.; 0.5 i.v. up to 3×p.d.; 0.5 r. up to 2×p.d.	0.5 o. i.m. i.v.	1.5 o. i.m. i.v.	0.5	1.5	
Aminophylline Injection (Injectabile (25% Aminophylline) Aminophyllini) (2.5% Aminophylline)	0.4–2 ml 4–20 ml					2 ml 20 ml	6 ml 60 ml	
Ammonium Chloride (Ammonium Chloratum)	0.3–4		1 4×p.d.			—	—	—

* In USA the name *Adrenalin* is a registered trade mark (PARKE, DAVIS).

Abbreviations:

alk.	alkaloids	gtt.	drops	min.	minimum	r.	rectal
B.P.	BRITISH PHARMACOPOEIA 1953	i.d.	initial dose	ml	millilitre or ccm	s.c.	subcutaneous
B.P.C.	BRITISH PHARMACEUTICAL CODEX 1954	i.m.	intramuscular	o.	oral	s.d.	single dose
c.d.	controlling dose	i.v.	intravenous	p.d.	per day	s.l.	sublingual
D.A.B.	DEUTSCHES ARZNEIBUCH 6	I.U.	international units	P.G.	PHARMACOPOEA GALLICA VII	tot.	total
div.	divided dose	m.d.	maintenance dose	P.H.	PHARMACOPOEA HELVETICA V	U.	units
emet.	emetic dose	mg	milligram	P.I.	PHARMACOPOEA INTERNATIONALIS	U.S.P.	UNITED STATES PHARMACOPEIA XV

	Usual Doses in grams (unless otherwise stated)				Maximal Doses in grams (unless otherwise stated)					
	B.P. or B.P.C.	U.S.P.	P.I., P.G., etc.		P.I.		P.H.		D.A.B.	
	oral unless otherwise stated					oral unless otherwise stated		oral or parenteral unless otherwise stated		
	single	single	single	per day	single	per day	single	per day	single	per day
Amodiaquine HCl*	0.2-0.6		0.20	0.4-1	—	—				
Amphetamine Sulphate (Amphetamini Sulfas)	0.0025-0.01	0.01 2 × p.d.	0.0025; 0.002 s.c.	up to 0.015; up to 0.01 s.c.	0.02; 0.005 s.c.	0.04; 0.03 s.c.	0.015	0.03		
Amyl Nitrite (Inhalant) (Amylis Nitris)	0.12-0.3 ml	0.3 ml	0.04-0.07	0.35	0.2	1	0.2	0.5	0.2	0.5
Amylene Hydrate (Amyleni Hydras)	2-4 ml	—	2-3 o. r.	up to 8 o. r.	—	—	4	8	4	8
Amylocaine HCl (Amylocainum HCl)							0.1	0.3		
Aneurine HCl, Vitamin B ₁ (Aneurinum HCl)	20-50 mg o. s.c. i.m.; 2-5 mg p.d. prophyl.; 20-50 mg p.d. therap.	2-50 mg o. s.c. p.d. therap.; 2 mg o. s.c. p.d. pregnancy	0.01-0.1 o. s.c.	up to 0.2 o. s.c.	—	—	—	—	—	
Antifebrin. See Acetanilide										
Antimony Potassium Tartrate (Stibii et Kalii Tartras)	0.002-0.008; 0.03-0.12 i.v.; 0.03-0.06 emet.	0.04 i.v. 3 × weekly	0.03-0.12 i.v.	0.12 i.v.	0.12 i.v.	0.2 i.v.	0.1	0.3	0.1	0.3
Antimony Sodium Tartrate (Stibii et Sodii Tartras)	0.002-0.008; 0.03-0.12 i.v.; 0.03-0.06 emet.		0.03-0.12 i.v.	0.12 i.v.	0.12 i.v.	0.2 i.v.				
Antipyrine. See Phenazone										
Apomorphine HCl (Apomorphinum HCl)	0.002-0.008 emet. s.c. i.m.	5 mg emet. s.c.	0.002- 0.005 s.c.	0.005 s.c.	0.005 s.c.	0.01 s.c.	0.02	0.05	0.02	0.06

Abbreviations:

alk. alkaloids
B.P. BRITISH PHARMACOPOEIA 1953
B.P.C. BRITISH PHARMACEUTICAL CODEX 1954
c.d. controlling dose
D.A.B. DEUTSCHES ARZNEIBUCH 6
div. divided dose
emet. emetic dose

ggt. i.d. i.m. i.v. I.U. m.d. mg
drops initial dose intramuscular intravenous international units maintenance dose milligram
min. ml o. p.d. P.G. P.H. P.I.
minimum millilitre or ccm oral per day PHARMACOPOEA GALICA VII PHARMACOPOEA HELVETICA V PHARMACOPOEA INTERNATIONALIS

r. rectal
s.c. subcutaneous
s.d. single dose
s.l. sublingual
tot. total
U. units
U.S.P. UNITED STATES PHARMACOPOEIA XV

	Usual Doses			Maximal Doses					
	in grams (unless otherwise stated)			in grams (unless otherwise stated)					
	B.P. or B.P.C.	U.S.P.	P.I., P.G., etc.	P.I.		P.H.		D.A.B.	
	single	single	single	oral unless otherwise stated	per day	oral or parenteral unless otherwise stated	single	per day	single
Belladonna Extract (0.5 % alk.) (Extractum Belladonnae) (1.0 % alk.) (1.5 % Hyosc.)	0.015-0.06		0.03	0.01	0.1	0.3	0.1	0.05	0.15
Belladonna Herb, Prepared (0.3 % alk.) (Pulvis Belladonnae Herbae)	0.03-0.2	—	0.05-0.10	0.10-0.20	0.2	0.6	0.2	0.2	0.6
Belladonna Root . . . (min. 0.45 % alk.) (Radix Belladonnae)	—	—	—	—	0.1	0.3	0.1	—	—
Belladonna Tincture (0.05 % alk.) (Tinctura Belladonnae) (0.03 % alk.)	0.6-2 ml	0.6 ml 3 × p.d.	0.2-0.6 ml 0.30-1	1-2	5	3	1	—	—
Benzene (Benzolum)	—	—	—	—	0.5	1.5	0.5	—	—
Benzyl Benzoate (Benzylis Benzoas)	0.3-0.5 ml	—	0.25	0.75	1.5	—	—	—	—
Bismuth Carbónate (Bismuthi Subcarbonas)	0.6-2	1 4 × p.d.	0.5	1.5	—	—	—	—	—
Bismuth Salicylate (Bismuthi Subsaliçylas)	0.6-2; 0.06-0.2 i.m.	0.1 i.m. weekly	0.5; 0.1 i.m.	1.5; 0.1 i.m.	—	—	—	—	—
Bitter-Almond Water (ca. 0.1 % HCN) (Aqua Amygdalarum Amararum)			0.5	—	—	—	—	2	6

Bromadalum. See Carbromal

Bromisovalum. See Bromvaletone

	0.03-0.12 ml		0.1	0.5	0.5	0.5	1.5	0.5	1.5	0.5	1.5
Bromoform (Bromoformium)											
Bromoform Solution .. (1 ml = 0.1 g (Bromoformium Solutum) Bromof.)								5	15		
Bromvalerone .. (Bromisovalum)			0.3	—				1	2	—	—
Bulbus Scillae. See Squill											
Butazolidin (GEIGY). See Phenylbutazone											
Caffeine .. (Coffeinum)	0.3-0.6	0.2	0.25 o. s.c.	0.5 o. s.c.	0.5 o. s.c.	1.5 o. s.c.	0.5	0.5	1.5	—	—
Caffeine and Sodium Benzoate .. (Coffeinum et Natrii Benzoas)	0.3-1.0; 0.12-0.3 s.c.	0.5 o. s.c.	0.5 o. s.c.	1 o. s.c.	1 o. s.c.	3 o. s.c.	1; 0.5 s.c.	—	3; 2 s.c.	—	—
Caffeine and Sodium Salicylate .. (Coffeinum et Natrii Salicylas)			0.4 s.c.	1 s.c.	1 s.c.	3 s.c.	1; 0.5 s.c.	—	3; 2 s.c.	—	—
Caffeine Citrate .. (Coffeinum Citricum)	0.12-0.6						0.75	2			
Calciferol, Vitamin D ₂ .. (Calciferolum)	0.025-0.1 mg p.d. prophyl. 1000-4000 U. p.d. prophyl. 0.125-1.25 mg p.d. therap. 5000-50,000 U. p.d. therap.	0.01 mg p.d.*	0.001	upto 0.015	0.015	0.015	0.015	0.9	0.015		
Calciferol Solution, Concentrated .. (Solutio Calcif. Conc.) (650,000 U./g)											
Calcium Chloride, Hydrated (6H ₂ O) ... (Calcium Chloratum)	0.6-2 i.v.		1	1-4	—	—	—	—	—	—	—
Calcium Gluconate .. (Calcii Gluconas)	1-4; 10% 10-20 ml i.v. i.m.	5 3 × p.d.; 1 i.v.	1; 1 i.v. i.m.	5; 2 i.v. i.m.	—	—	—	—	—	—	—
Calcium Lactate .. (Calcii Lactas)	1-4		1	5	—	—	—	—	—	—	—
Cambogia .. (Gutti)			0.1-0.2	—	—	—	0.2	0.3	0.6	1	
Camoquine. See Amodiaquine											
Camphor .. (Camphora)	0.12-0.3	—	0.1-0.2 s.c. i.m.	up to 1 s.c. i.m.	1 s.c. i.m.	5 s.c. i.m.	—	—	—	—	—
Camphor, Monobromated .. (Camphora Monobromata)			0.25	0.5			0.2		1		

* In rickets 0.03-0.0375 mg p.d.; in hypocalcaemic tetany 5 mg p.d.

Abbreviations:

alk. alkaloids
B.P. BRITISH PHARMACOPOEIA 1953
B.P.C. BRITISH PHARMACEUTICAL CODEX 1954
c.d. controlling dose
D.A.B. DEUTSCHES ARZNEIBUCH 6
div. divided dose
emet. emetic dose

	Usual Doses						Maximal Doses					
	in grams (unless otherwise stated)						in grams (unless otherwise stated)					
	B.P. or B.P.C.	U.S.P.	P.I., P.G., etc.			oral unless otherwise stated	P.I.	P.H.			oral or parenteral unless otherwise stated	D.A.B.
	single	single	single	single	per day		single	single	per day	single		
Cantharides (0.6% P.H., (Cantharis) min. 0.7% D.A.B., Cantharidin) Cantharidin (Cantharidinum)								0.03	0.06	0.05		
Cantharidin Solution (0.05% P.H., (Tinctura Cantharidis) 0.07% D.A.B., Cantharidin)								0.0002	0.0002			
Carbachol (Carbacholum)	0.001-0.004; 0.25-0.5 mg s.c.	—	0.002; 0.0002 s.c.	0.006; 0.0006 s.c.	0.012; 0.0012 s.c.	0.004; 0.0004 s.c.		0.3	0.6	0.5	1.5	
Carbarone (Carbarsonum)	0.12-0.25	0.25 2 × p.d. for 10 days; 0.13 vaginal	0.1-0.25	0.2-0.5		—						
Carbolic Acid. See Phenol												
Carbon Tetrachloride (Carbonei Tetrachloridum)	2-4 ml s.d.		2.50	2.50	2.50	2.50						
Carbromal (Bromadalum)	0.3-1		0.25-0.5	—				1.5	3	—	—	
Castor Oil (Oleum Ricini)	4-16 ml	15 ml	5-30	5-30				—	—	—	—	
Chenopodium Oil (Aetheroleum Chenopodii)	0.2-1 ml		0.25	0.5	0.5	0.5	1	0.5	1	0.5	1	
Cherry-Laurel Water (ca. 0.1% HCN) (Aqua Laurocerasi)			0.5-1	3				2	6	—	—	

Chininum. See Quinine

Usual and Maximal Doses (continued)										
Chiniofon Sodium (Chiniofonum)	0.1-0.5; 1-5 r.	0.25 3×p.d. for 7 days	0.5; 1 r.	1.5; 3 r.	1; 2 r.	3; 6 r.	3	6	3	6
Chloral Hydrate (Chlorali Hydras)	0.3-2	0.6 up to 3×p.d.	1	3	2	6	3	6	3	6
Chloramphenicol	1.5-4 p.d. div.	3 p.d.	0.25-0.50	2-3	—	—	—	—	—	—
Chlorbutol (Alcohol Trichlorisobutylicus)	0.3-1.2	—	—	—	—	—	—	—	—	—
Chlorguanide. See Proguanil										
Chloroform (Chloroformium Anaestheticum)	0.06-0.3 ml	—	0.1	0.3	0.5	1.5	0.5	1.5	0.5	1.5*
Chloroquine Phosphate** (Chloroquini Diphosphas)	0.5 weekly (prophyl.)	0.5 weekly (prophyl.)	0.3	0.3-0.6	—	—	—	—	—	—
Chlortetracyclin HCl	1-2 p.d. div.	0.25 4×p.d.	0.25-0.50	1.50-3	—	—	—	—	—	—
Coca (Folium Cocae)	(min. 0.7% alk.)						3	6	3	6
Coca Extract, Liquid (Extractum Cocae fluidum)	(1% alk.)		0.5-2 ml	—			3	6	3	6
Cocaine (Cocainum)	—						0.03	0.06	—	—
Cocaine Hydrochloride (Cocainum HCl)	0.008-0.016	—	0.01	0.02	0.03	0.06	0.03	0.06	0.05	0.15
Cocaine Nitrate (Cocaini Nitras)			0.01	0.02	0.03	0.06	0.03	0.06	0.05	0.15
Codeine (Codeinum)	0.01-0.06		0.02	0.06	0.1	0.3	0.1	0.3		
Codeine HCl (Codeinum HCl)							0.1	0.3		
Codeine Phosphate (Codeini Phosphas)	0.01-0.06	0.03 every 4 hours	0.03	0.1	0.15	0.4	0.1	0.3	0.1	0.3

* Ingestion.
** Minimum effective dose in malaria 0.45 g. Therapeutic doses: B.P., 1.0, then 0.5 p.d.; U.S.P., 1.0, then 0.5 after 6 hours and on 2nd and 3rd days.
Antiprotozoan doses: B.P., 0.5-1 p.d.; U.S.P., 1.5 p.d. for 2 weeks, then 0.75 twice weekly for several months. See also footnote on page 371.

Abbreviations:

alk. alkaloids
B.P. BRITISH PHARMACOPOEIA 1953
B.P.C. BRITISH PHARMACEUTICAL CODEX 1954
c.d. controlling dose
D.A.B. DEUTSCHES ARZNEIBUCH 6
div. divided dose
emet. emetic dose

gtt. drops
i.d. initial dose
i.m. intramuscular
i.v. intravenous
I.U. international units
m.d. maintenance dose
mg milligram

min. minimum
ml millilitre or ccm
o. oral
p.d. per day
P.G. PHARMACOPOEA GALLICA VII
P.H. PHARMACOPOEA HELVETICA V
P.I. PHARMACOPOEA INTERNATIONALIS

r. rectal
s.c. subcutaneous
s.d. single dose
s.l. sublingual
tot. total
U. units
U.S.P. UNITED STATES PHARMACOPEIA XV

	Usual Doses in grams (unless otherwise stated)				Maximal Doses in grams (unless otherwise stated)					
	B.P. or B.P.C.	U.S.P.	P.I., P.G., etc.		P.I.		P.H.		D.A.B.	
	oral unless otherwise stated					oral unless otherwise stated		oral or parenteral unless otherwise stated		
	single	single	single	per day	single	per day	single	per day	single	per day
Codeine Phosphate Tablets (Compressi Codeini Compositi) (0.02 g Codeine Phosphate)	—	—					No V	No XV		
Codeine Tablets, Compound (Compressi Acidi Acetylosalicylici Compositi)	No I-II		No I-II	—			No II	No VI		
Cod-Liver Oil (Oleum Jecoris Aselli)	4-12 ml p.d. div.	4 ml	15	30	—	—	—	—		
Cod-Liver Oil, Phosphorated (0.01% (Oleum]ecoris Phosphorat.) Phosph.)							10	30		
Colchicine (Colchicinum)	0.5-1 mg; 2-8 mg tot.	0.0005 every ½-1 hour	0.0005	0.001	0.002	0.006	0.001	0.003	0.002	0.005
Colchicum Extract, Liquid (Extractum Colchici) (0.5% Colchicine)	—						0.2	0.6		
Colchicum Seed (0.4% Colchicine) (Semen Colchici)	—		—	—	—	—	0.25	0.75	—	—
Colchicum Seed, Powdered (Pulvis Colchici) (0.4% Colchicine)	—		—	—	—	—	0.25	0.75		
Colchicum Tincture (Tinctura Colchici) (P.I. 0.04%, P.H. 0.05%, D.A.B. min. 0.04%, B.P. 0.03% Colchicine)	0.3-1 ml		0.50-1	1.50-3	3	12	1	6	2	6

Drug	Dose	Frequency	Route	Form	Concentration	Strength	Quantity	Notes
Colocynth (Fructus Colocynthis)	0.3-0.6 emet.	—	—	—	—	—	1	0.3
Colocynth Extract (Extractum Colocynthis)	—	—	—	—	—	—	0.05	0.15
Colocynth Tincture (Tinctura Colocynthis)	—	—	—	—	—	—	1	3
Copper Sulphate (Cuprum Sulfuricum)	0.3-0.6 emet.	—	—	—	—	—	1	—
Cotarnine Chloride (Cotarninium chloratum)	—	—	—	—	—	—	0.1	0.3
Creosote (Creosotum)	0.12-0.6 ml	—	—	—	—	—	0.25	1.5
Creosote Carbonate (Creosotum Carbonicum)	—	—	—	—	—	—	1	—
Creosote Pills (Pillulae Creosoti)	—	—	—	—	—	—	No V	No XX
Croton Oil (Oleum Crotonis)	—	—	—	—	—	—	0.05	0.15
Crystal Violet (Viola Crystallina)	0.01-0.03	—	—	—	—	—	—	—
Cyanocobalamin, Vitamin B ₁₂ (Cyanocobalaminum)	0.05-0.1 mg i.d. weekly i.m.; 0.05-0.1 mg m.d. every 2-3 weeks i.m.	—	—	—	—	—	—	—
Cyclobarbitone (Cyclobarbitalum)	0.2-0.4	—	—	—	—	—	—	—
Cyclobarbitone Calcium	—	—	—	—	—	—	0.3	0.4
Deoxycortone Acetate (Desoxycortoni Acetas)	2-5 mg p.d. i.m.; Implants 0.1-0.4 tot.	—	—	—	—	—	—	—
Dicoumarol (Dicoumarolum)	0.05-0.3 p.d.	—	—	—	—	—	—	—
Dienoestrol	0.0005-0.01 p.d.	—	—	—	—	—	—	—
Diethylstilboestrol. See Stilboestrol	—	—	—	—	—	—	—	—
Digitalis Extract (1 g = 3.3 g Fol.Dig.) (Extractum Digitalis)	—	—	—	—	—	—	0.06	0.3
Digitalis, Prepared (1 g = 10 I.U.) (Pulvis Digitalis Folii Standard.)	0.03-0.1	—	—	—	—	—	0.2	1

Abbreviations:

alk. alkaloids
B.P. BRITISH PHARMACOPOEIA 1953
B.P.C. BRITISH PHARMACEUTICAL CODEX 1954
c.d. controlling dose
D.A.B. DEUTSCHES ARZNEIBUCH 6
div. divided dose
emet. emetic dose

gtt. drops
i.d. initial dose
i.m. intramuscular
i.v. intravenous
I.U. international units
m.d. maintenance dose
mg milligram

min. minimum
ml millilitre or ccm
o. oral
p.d. per day
P.G. PHARMACOPOEA GALLICA VII
P.H. PHARMACOPOEA HELVETICA V
P.I. PHARMACOPOEA INTERNATIONALIS

r. rectal
s.c. subcutaneous
s.d. single dose
s.l. sublingual
tot. total
U. units
U.S.P. UNITED STATES PHARMACOPEIA XV

	Usual Doses			Maximal Doses		
	in grams (unless otherwise stated)			in grams (unless otherwise stated)		
	B.P. or B.P.C.	U.S.P.	P.I., P.G., etc.	P.I.	P.H.	D.A.B.
	oral unless otherwise stated			oral unless otherwise stated		
	single	single	single	single	per day	single
Digitalis Tincture (1 ml = 1 I.U.) (Tinctura Digitalis) (1 g = 0.1 g Dig.)	0.3-1 ml		0.5-1	1.5	6	1.5
Digoxin (Digoxinum)	1-1.5 mg i.d.; 0.25 mg 1-2 x p.d. m.d.; 0.5-1 mg i.d. i.v.	1.5 mg (3 mg p.d.) i.d.; 0.5 mg p.d. m.d.*	0.0005-0.001; 0.0005 i.v.	0.001	0.002	5
Dihydrocodeinone Bitartrate (Dihydrocodeinonum Bitartaricum)			0.01	0.001 i.v.	0.0015 i.v.	0.015
Dihydrohydroxycodone HCl (Dihydroxycodoneinum HCl)			0.01 o. s.c.			0.03; 0.02 s.c.
Dihydromorphinone HCl (Dihydromorphinonum HCl)		0.002 o. s.c. every 4 hours	0.002; 0.001-0.002 s.c.	0.005 s.c.	0.015 s.c.	0.1; 0.06 s.c.
Dihydrostreptomycin (Dihydrostreptomycinum)	1 p.d. (base) i.m.	0.5 p.d. (base) i.m.	0.50-1 i.m.	—	—	0.005; 0.003 s.c.
Diiodotyrosine (Diiodotyrosinum)				0.3	0.6	
Dimercaprol, BAL	0.2 i.m. div. 1st day; then according to need	0.01/kg i.m. p.d. div. 2 days; then reduced	0.15-0.30 i.m.	0.30 i.m.	1.50 i.m.	
Dimethylaminoantipyrine. See Amido-pyrine						
Diphenylhydantoin. See Phenytoin						
Dover's Powder. See Ipecacuanha and Opium Powder						

	0.03–0.06 p.d. s.c. i.m.	0.001/kg (max. 0.06) s.c. p.d.	0.04 s.c.	0.08 s.c.	0.1 s.c.	0.1 s.c.	0.1	0.2	0.05	0.1
Emetine HCl (Emetinum HCl)										
Emetine and Bismuth Iodide (Emetinae et Bismuthi Iodidum)	0.06–0.2 p.d.									
Ephedrine HCl (Ephedrinum HCl)	0.016–0.06		0.01 o. s.c.	0.03; 0.02 s.c.	0.05; 0.04 s.c.	0.15; 0.12 s.c.	0.1	0.3		
Epinephrine. See Adrenaline										
Ergometrine Maleate (Ergometrini Maleas)	0.5–1 mg; 0.25–1 mg i.m.; 0.125–0.5 mg i.v.	0.0002 o. i.v. i.m.	0.0005; 0.00025 s.c. 0.00025 i.v.	0.0015; 0.00075 s.c. 0.00075 i.v.	0.001; 0.0005 s.c. 0.0005 i.v.	0.002; 0.001 s.c. 0.001 i.v.		0.001; 0.0005 s.c. 0.001 s.c.		
Ergometrine Tartrate (Ergometrini Tartras)										
Ergonovine. See Ergometrine										
Ergot (Secale Cornutum)	—		0.5	—			1	4	—	—
Ergot, Prepared (Pulvis Secalis Cornuti Standard.)	0.15–0.5		0.5	—	1	5				
Ergot Extract (1 g = 2 g Ergot) (Extractum Secalis Cornuti)							0.5	1.5		
Ergotamine Tartrate (Ergotamini Tartras)	0.001–0.002 s.d.; 0.00025–0.0005 s.c. i.m.	2 mg, then 1 mg/½ hour; 0.25 mg i.m.	0.00025 o. s.c.	upto 0.001 o. s.c.	0.0005 o. s.c.	0.002 o. s.c.				
Eserine. See Physostigmine										
Ethinylloestradiol (Aethisteronum)	0.01–0.1 mg p.d. 0.025–0.1 p.d.	0.05 mg p.d. 0.01 up to 4 × p.d.	10–20 µg 0.005	20–100 µg 0.025	— —	— —	— —	— —		
Ethyl Biscoumacetate (<i>Tromexan</i> GEIGY)	0.15–1 p.d. according to prothrombin activity									
Ethylhydrocupreine (Aethylhydrocupreinum)							0.25	0.75		
Ethylhydrocupreine HCl (Aethylmorphinum HCl)	0.006–0.03	—	0.02	0.05			0.25	0.75	0.1	0.3

* Doses i.v.: 1 mg i.d., 0.5 mg m.d.

Abbreviations:

- alk.
alkaloids
- B.P.
BRITISH PHARMACOPOEIA 1953
- B.P.C.
BRITISH PHARMACEUTICAL CODEX 1954
- c.d.
controlling dose
- D.A.B.
DEUTSCHES ARZNEIBUCH 6
- div.
divided dose
- emet.
emetic dose

- gtt.
i.d.
i.m.
i.v.
I.U.
m.d.
mg
- drops
initial dose
intramuscular
intravenous
international units
maintenance dose
milligram
- min
ml
o.
p.d.
P.G.
P.H.
P.I.
- minimum
millilitre or ccm
oral
per day
PHARMACOPOEA GALLICA VII
PHARMACOPOEA HELVETICA V
PHARMACOPOEA INTERNATIONALIS
- r.
s.c.
s.d.
s.l.
tot.
U.
U.S.P.
UNITED STATES PHARMACOPOEIA XV
- rectal
subcutaneous
single dose
sublingual
total
units

	Usual Doses in grams (unless otherwise stated)						Maximal Doses in grams (unless otherwise stated)					
	B.P. or B.P.C.		U.S.P.		P.I., P.G., etc.		P.I.		P.H.		D.A.B.	
	oral unless otherwise stated						oral unless otherwise stated		oral or parenteral unless otherwise stated			
	single		single		single	per day	single	per day	single	per day	single	per day
<i>Eukodal</i> (MERCK). See Dihydro- hydroxycodine HCl												
Extractum Scillae. See Squill Extract												
Extractum Strychni. See Nux Vomica Extract												
Ferri et Ammonii Citras. See Iron and Ammonium Citrate												
Ferrous Sulphate (Ferrosi Sulfas)	0.2-0.3		0.3 3 × p.d.		0.2	0.6	—		—		—	
Ferrous Sulphate Exsiccated (Ferrosi Sulfas Exsiccatus)	0.06-0.2		0.2 3 × p.d.		0.1	0.3	—		—		—	
Filicin Extract (25 % Filicin) (Extractum Filicis)										10		10
Filicin Extract, conc. (Extractum Filicis Concentratum)					2.5 p.d. tot.	2.5 p.d. tot.			3			
Folic acid	0.005-0.02 p.d.		0.01 p.d.		0.005-0.01; 0.002- 0.005 i.m. i.v.	0.02-0.05; 0.01-0.02 i.m. i.v.	—		—			
FOWLER'S Solution. See Arsenical Solution												
Glyceryl Trinitrate Solution (1%) (Nitroglycerinum Solutum)	0.05-0.1 ml				0.03-0.08	0.08-0.16			0.4	0.1		0.4

Guaiacol	0.25	0.75			0.25	1	—	—
(Guaiacolum)								
Guaiacol Carbonate	0.3	1			1	3	—	—
(Guaiacolum Carbonicum)								
Gutti. See Cambogia								
Halibut-Liver Oil	0.05	up to 0.5	—	—	—	No IV	0.25	—
(Oleum Jecoris Hippoglossi)	0.1 ml p.d. prophylactic							
Heim's Pills						No XII		
(Pilulae Hydragogae Heimii)								
Heparin	5000 U. par- enteral	6000 U. i.v. up to 60000 U. i.v.	—	—	—			
(Heparinum)								
Hexobarbitone	0.25	—	—	—	0.5	1.5		
(Hexobarbitalum)	0.25-0.5							
Hexobarbitone Sodium	up to 1 i.v.	—	1	1	1.0 i.v.	—		
(Hexobarbitalum Solubile)	0.2-1 i.v. i.m.; 40 mg/kg r. (max. 2)							
Histamine Acid Phosphate	0.0003 s.c.	0.0005 s.c.	0.001 s.c.	0.001 s.c.	0.002 s.c.			
(Histamini Phosphas)								
Histamine Dihydrochloride						0.006; 0.002 s.c.	0.006; 0.006 s.c.	
(Histaminum Dihydrochloricum)								
Homatropine HBr	—	0.0005	0.002	0.001	0.003	0.003	0.001	0.003
(Homatropinum HBr)								
Hydnocarpus Oil	0.3-1 ml rising to 4 ml; 2 ml rising to 5 ml s.c.i.m.	—	As in B.P.	—	—	3	0.5	
(Oleum Hydnocarpi)								
Hydrastinine Chloride	0.02	0.08			0.03	0.1	0.05	0.15
(Hydrastininum Hydrochloricum)								
Hydrastis					1	4		
(Rhizoma Hydrastidis)								
Hydrastis Extract, Liquid (2% Hydrastine)					1	4		
(Extractum Hydrastidis Fl.)								
Hydrastis, Powdered (2% Hydrastine)					1	4		
(Pulvis Hydrastidis)								

Abbreviations:

alk. alkaloids
B.P. BRITISH PHARMACOPOEIA 1953
B.P.C. BRITISH PHARMACEUTICAL CODEX 1954
c.d. controlling dose
D.A.B. DEUTSCHES ARZNEIBUCH 6
div. divided dose
met. emetic dose

	Usual Doses						Maximal Doses					
	in grams (unless otherwise stated)						in grams (unless otherwise stated)					
	B.P. or B.P.C.	U.S.P.	P.I., P.G., etc.			oral unless otherwise stated	P.I.	P.H.			oral or parenteral unless otherwise stated	D.A.B.
	single	single	single	single	per day		single	single	per day	single		
Hydrochloric Acid, Dilute (10% HCl) (Acidum Hydrochloricum Dilutum)	0.6-8 ml		2	4	4	4	12	—	—	—	—	—
Hydromorphone. See Dihydromor- phinone												
Hyoscine HBr (Hyoscinum HBr)	0.0003-0.0006 o. s.c.	—	0.0001- 0.0005 s.c.	0.00025- 0.0005 s.c.	0.0005 o. s.c.	0.0005 s.c.	0.001 s.c.	0.0005	0.003	0.001	0.003	0.003
Hyoscyamine Sulphate (Hyoscyaminum Sulfuricum)			0.0002 o. s.c.	0.0005 o. s.c.	0.0005 o. s.c.			0.0005	0.0015			
Hyoscyamus (min. 0.05% alk.) (Hyoscyami Herbae) (min. 0.07% alk.)	—		0.1-0.2	0.3-0.5				1	3	0.4	1.2	
Hyoscyamus Extract ... (0.3% alk.) (Extractum Hyoscyami) (0.5% alk.)	0.016-0.06							0.1	0.3	0.15	0.5	
Hyoscyamus, Powdered (0.05% alk.) (Pulvis Hyoscyami Herbae)	—		0.1-0.2	0.3-0.5		0.5	1.5					
Hyoscyamus Tincture (0.05% alk.) (Tinctura Hyoscyami) (0.005% alk.)	2-4 ml		1-2	3-5		5	15	1	3			
odine (in solution) (Iodum)	—		0.01-0.02	0.05		0.05	0.15	—	—	—	—	—
Iodine Tincture ... (7.0% I, 3.0% KI) (Tinctura Iodi) (2.5% I, 2.5% KI)	0.3-2 ml							—	—	0.2	0.6	
Iodoform (Iodoformium)	—							0.2	0.6	—	—	—
Ipecacuanha (2% alk.) (Radix Ipecacuanhae)	—	—	0.05-1	0.05-1				2	4	—	—	—

	0.3-0.6		0.05-1	0.05-1	0.05-1		1	4	1.5	5
Ipecacuanha and Opium Powder (Pulvis Ipecacuanhae Opiatus) (1.0% Morphine)							1	4		
Ipecacuanha and Opium Powder, Soluble (Pulvis Ipecacuanhae Opiatus Sol.) (1.0% Morphine)							1	4		
Ipecacuanha Extract (Extractum Ipecacuanhae) Dry (2% alk.) Liquid (2% alk.)	0.03-0.12 ml	0.5 ml emet.	0.01-0.06	—	—		2	4		
Ipecacuanha, Prepared . . (2.0% alk.) (Pulvis Ipecacuanhae Radicis Stand.)	0.03-0.12; 1-2 emet.		0.05-1	0.05-1	2	2	2	4		
Iron and Ammonium Citrate (Ferri et Ammonii Citras)	1-3		1	3 up to 6	—	—	—	—		
Isoprenaline Sulphate (Isoprenalinae Sulfas)	0.005-0.02		0.01-0.02; 0.01-0.015 s.l.	0.06; 0.015- 0.045 s.l.	—	—	—	—		
Jaborandi (Folium Jaborandi)							2	6		
Jalap Resin (Resina Jalapae)	0.06-0.3		0.2-0.5	—	—	—	0.5	1.5	—	—
Kalium. See Potassium										
Kalium Arsenicosum Sol. See Arsenical Solution										
Kola Extract (10% Caffeine + (Extractum Colae) Theobromine)							4.5	15		
Lactylphenetidine (Phenetidinum Lactylatum)							1	3	—	—
Lanatoside C (Lanatosidum C)			0.0005 o. i.v.	0.001 o. i.v.	0.001 o. i.v.	0.001 o. i.v.				
Lead Acetate (Plumbum Aceticum)	—						0.1	0.3	0.1	0.3
Leptazol (Pentetrazolum)	0.05-0.1 s.c. i.v. i.m.		0.1 o. s.c. i.m. i.v.	0.3 o. s.c. i.m. i.v.	—	—	—	—		

Abbreviations:

alk.	alkaloids	gtt.	drops	min.	minimum	r.	rectal
B.P.	BRITISH PHARMACOPOEIA 1953	i.d.	initial dose	ml	millilitre or ccm	s.c.	subcutaneous
B.P.C.	BRITISH PHARMACEUTICAL CODEX 1954	i.m.	intramuscular	o.	oral	s.d.	single dose
c.d.	controlling dose	i.v.	intravenous	p.d.	per day	s.l.	sublingual
D.A.B.	DEUTSCHES ARZNEIBUCH 6	I.U.	international units	P.G.	PHARMACOPOEA GALICA VII	tot.	total
div.	divided dose	m.d.	maintenance dose	P.H.	PHARMACOPOEA HELVETICA V	U.	units
emet.	emetic dose	mg	milligram	P.I.	PHARMACOPOEA INTERNATIONALIS	U.S.P.	UNITED STATES PHARMACOPEIA XV

	Usual Doses in grams (unless otherwise stated)				Maximal Doses in grams (unless otherwise stated)				
	B.P. or B.P.C.	U.S.P.	P.I., P.G., etc.		P.I.	P.H.		D.A.B.	
	oral unless otherwise stated			oral or parenteral unless otherwise stated					
	single	single	single	per day	single	per day	single	per day	
Lobelia (min. 0.3% alk.) (Herba Lobeliae)	0.2-0.6					0.1	0.3	0.1	0.3
Lobelia Tincture (0.05% alk.) (Tinctura Lobeliae)						0.5	2	1	3
Lobeline HCl (Lobelinum HCl)	0.003-0.009 i.m.		0.01 s.c. 0.003 i.v.	0.02 s.c. up to 0.01 i.v.	0.02 s.c. 0.006 i.v.	0.01 s.c.	0.02 s.c.	0.02	0.1
Magnesium Trisilicate (Magnesii Trisilicas)	0.3-2	1 4 × p.d.							
Male Fern Extract (10% Filicin) (Aspidinofilicinum Oleo Solutum)			10	—				20	20
Male Fern Extract (25% Filicin) (Oleoresina Filicis Maris)	3-6 ml	5	0.5	6-8	10	10			
Mecholyl Chloride. See Methacholine Chloride									
Menaphthone, Menadione (Menadionum)	0.001-0.005 p.d. i.m.	0.002 p.d.	0.001- 0.002o.i.m.	0.001- 0.002o.i.m.	0.002o.i.m.	0.01 o. i.m.			
Mepacrine HCl* (Mepacrine Hydrochloridum)	0.2-0.5 p.d. div. therap.; 0.1 p.d. div. prophyl.	0.1 prophyl.**	0.1	0.2-0.5	—	—	—	—	—
Mepacrine Methanesulphonate* (Mepacrine Methanosulfonas)	0.1-0.3 i.m.		0.1 i.m.	0.1-0.3 i.m.	—	—	—	—	—
Meperidine. See Pethidine									

Mepyramine Maleate (Mepyraminae Maleas)	0.3-0.8 p.d. div.	—	0.05-0.10; 0.05 i.m. i.v.	up to 0.50; up to 0.20 i.m. i.v.	—	—	—	—	—	—
Mercuric Chloride (Hydrargyri Bichloridum)	0.002-0.004	—	0.005-0.01 i.m. i.v.	0.01-0.02	0.015	0.03	0.02	0.06	0.02	0.06
Mercuric Cyanide (Hydrargyri Cyanidum)			0.004- 0.008 i.v.	—	—	—	—	—	0.01	0.03
Mercuric Iodide, Red (Hydrargyri Iodidum Rubrum)	0.002-0.004		0.01	—	0.02	0.04	0.02	0.06	0.02	0.06
Mercuric Oxide, Red (Hydrargyri oxydum Rubrum)							0.02	0.1	0.02	0.06
Mercuric Oxide, Yellow (Hydrargyri oxydum Flavum)	—		—	—	—	—	0.02	0.06	0.02	0.06
Mercuric Oxycyanide (Hydrargyri Oxycyanidum)	—		—	—	—	—	0.01 s.c.	0.02 s.c.	0.01	0.03
Mercurous Chloride (Hydrargyri Subchloridum)	0.03-0.2		0.01-0.2	0.01-0.2	0.25	0.5	0.2	0.6	0.1 s.c.	—
Mercurous Iodide, Yellow (Hydrargyri Iodidum Flavum)	—		0.01-0.03	0.1			0.05	0.2		
Mercury (Hydrargyrum)	2-4 p.d. (syphilis)		0.05; 0.075 r.; 0.02-0.1 i.m.	0.1; 0.15 r.; 0.02-0.1 i.m.	0.1; 0.15 r.; 0.1 i.m.	0.3; 0.5 r.; 0.3 i.m.	—	—	—	—
Mercury Ointment, Grey (30% Hg) (Unguentum Hydrargyri Cinereum cut.)	—						—	5	—	—
Mercury Salicylate (Hydrargyri Salicylas)							0.02	0.1	0.15	—
Mersalyl (Mersalylum)	—		0.1-0.2 i.m. i.v.	0.1-0.2 i.m. i.v.	—	—				
Methacholine Chloride (Methacholinae Chloridum)	0.1-0.2; 0.01-0.025 s.c.	0.02 s.c.								
Methadone HCl	0.005-0.01	0.0075 o. s.c. every 4 hours	0.0075; 0.0025- 0.01 s.c. i.m.	up to 0.05; up to 0.03 s.c. i.m.	0.015 s.c. i.m.	0.045 s.c. i.m.	0.02	0.06		

* See footnote on page 371. ** Therapeutic doses: antimalarial and antiprotozoan: 0.2 every 6 hours for 5 doses, then 0.1 3 x p.d. for 6 days; anthelmintic: 0.5 + 0.5 sodium bicarbonate s.d.

Abbreviations:

alk.	alkaloids	ggt.	drops	min.	minimum	r.	rectal
B.P.	BRITISH PHARMACOPOEIA 1953	i.d.	initial dose	ml	millilitre or ccm	s.c.	subcutaneous
B.P.C.	BRITISH PHARMACEUTICAL CODEX 1954	i.m.	intramuscular	o.	oral	s.d.	single dose
c.d.	controlling dose	i.v.	intravenous	p.d.	per day	s.l.	sublingual
D.A.B.	DEUTSCHES ARZNEIBUCH 6	I.U.	international units	P.G.	PHARMACOPOEA GALLICA VII	tot.	total
div.	divided dose	m.d.	maintenance dose	P.H.	PHARMACOPOEA HELVETICA V	U.	units
emet.	emetic dose	mg	milligram	P.I.	PHARMACOPOEA INTERNATIONALIS	U.S.P.	UNITED STATES PHARMACOPOEIA XV

	Usual Doses in grams (unless otherwise stated)				Maximal Doses in grams (unless otherwise stated)					
	B.P. or B.P.C.	U.S.P.	P.I., P.G., etc.		P.I.	P.H.	D.A.B.			
			single	per day			single	per day	single	per day
oral unless otherwise stated		single	per day	oral unless otherwise stated	single	per day	oral or parenteral unless otherwise stated	single	per day	
Methoin	0.05-0.1									
Methylatropine HBr (Methylatropinium Bromatum)			0.001	0.002		0.001	0.003			
Methylene Blue	0.06-0.3		0.05	0.2		0.2	0.6			
(Methylthioninae Chloridum)										
Methyl Salicylate	—					2	6		—	—
(Methylum Salicylicum)										
Methylphenobarbitone	0.06-0.2					0.3	0.6			
(Methylphenobarbitonum)										
Methylsulphonal						1	2		1	2
(Methylsulfonylum)										
Methyltestosterone	0.025-0.05 p.d. men; 0.005-0.02 p.d. women	0.01 3 x p.d.; 0.005 up to 4 x p.d. s.l.	0.01; 0.005 s.l.	up to 0.05; up to 0.05 s.l.	—	—	—			
(Methyltestosteronum)										
Methylthiouracil	0.2-0.6 p.d. c.d.; 0.05-0.2 p.d. m.d.	0.05 4 x p.d.				0.15	0.5			
(Methylthiouracilum)										
Morphine HCl	0.008-0.02	0.015 o. s.c. (every 4 hours)	0.01 o. s.c.	—	0.02 o. s.c.	0.03 o. s.c.; 0.02 s.c.	0.1; 0.06 s.c.		0.03	0.1
(Morphinum HCl)										
Morphine Sulphate	0.008-0.02		0.01 o. s.c.	—	0.02 o. s.c.	0.03 o. s.c.				
(Morphini Sulfas)										
Naphthalene						0.5	3		—	—
(Naphthalinum Purum)										

[illegible]

Abbreviations:

alk. alkaloids
B.P. BRITISH PHARMACOPOEIA 1953
B.P.C. BRITISH PHARMACEUTICAL CODEX 1954
c.d. controlling dose
D.A.B. DEUTSCHES ARZNEIBUCH 6
div. divided dose
emet. emetic dose

gtt. drops
i.d. initial dose
i.m. intramuscular
i.v. intravenous
I.U. international units
m.d. maintenance dose
mg milligram

min. minimum
ml millilitre or ccm
o. oral
p.d. per day
P.G. PHARMACOPOEA GALLICA VII
P.H. PHARMACOPOEA HELVETICA V
P.I. PHARMACOPOEA INTERNATIONALIS

r. rectal
s.c. subcutaneous
s.d. single dose
s.l. sublingual
tot. total
U. units
U.S.P. UNITED STATES PHARMACOPOEIA XV

	Usual Doses			Maximal Doses		
	in grams (unless otherwise stated)			in grams (unless otherwise stated)		
	B.P. or B.P.C.	U.S.P.	P.I., P.G., etc.	P.I.	P.H.	D.A.B.
	oral unless otherwise stated			oral or parenteral unless otherwise stated		
	single	single	single	single	per day	single
Oestradiol Monobenzoate (Oestradioli Benzoas)	0.001-0.005 p.d. i.m.	0.001 i.m. p.d.	0.001- 0.005 i.m.	—	—	—
Oestrone (Oestronum)	0.001-0.01 p.d.; 0.1-1 mg i.m.	0.2-1 mg i.m.	0.001-0.01 i.m.	—	—	—
Oleoresina Filicis Maris. See Male Fern Extract						
Oleum Jecoris Aselli. See Cod-Liver Oil						
Oleum Jecoris Hippoglossi. See Halibut-Liver Oil						
Oleum Ricini. See Castor Oil						
Opial. See Papavaretum						
Opium Concentratum. See Papavaretum						
Opium Extract, Dry (20% Morphine) (Extractum Opii)	0.016-0.06		0.015-0.05	0.1	0.3	0.075
Opium Injection (1 ml = 0.01 g (Injectabile Opiali) Morphine)				2 ml	6 ml	
Opium, Powdered .. (10% Morphine) (Pulvis Opii Standard.)	0.03-0.2	—	0.1	0.2	0.6	0.15
Opium Tincture (1% Morphine) (Tinctura Opii)	0.3-2 ml	0.6 ml 4 x p.d.	0.5-1	2	6	1.5

	2-4 ml	4 ml 4 × p.d.	5-20	—	40	100	2	6	1.5	5
Opium Tincture, Camphorated (0.05% (Tinctura Opii Benzoica) Morphine)										
Opium Tincture, Saffron (1% Morphine) (Tinctura Opii Crocata)										
Orthocaine (Orthocaina)	—						1	3		
Ouabain, Strophanthin-G (Ouabainum)	0.00012-0.00025 i.v.	0.0005 i.v.	0.001; 0.00025 i.v.	up to 0.005; 0.0005 i.v.	0.005; 0.0005 i.v.	0.02; 0.001 i.v.			0.001	0.005
Oxytetracycline HCl	1-2 p.d. i.v. infusion; 0.2-0.4 p.d. i.m.	1 p.d. div.; 0.5 p.d. i.v.	0.25-0.50	1-3	—	—				
Oxytocin Injection (Injectio Oxytocini)	2-5 U. s.c. i.m.	10 U. i.m.	5-10 U. s.c. i.m.	5-10 U. s.c. i.m.	—	—				
Pamaquine* (Pamaquinum)	0.01-0.02		0.01	0.02 up to 0.06	—	—				
Papaveretum (50% Morphine) (Opium Concentratum)	0.01-0.02 o. s.c.						0.05; 0.04 s.c.	0.15; 0.12 s.c.	0.03	0.1
Papaverine HCl (Papaverinum HCl)	0.12-0.25	0.03 i.m. i.v.	0.05 o. s.c.	up to 0.25 o. s.c.	0.25 o. s.c.	1 o. s.c.	0.3; 0.05 s.c.	1.2; 0.15 s.c.	0.2	0.6
Paraldehyde (Paraldehydum)	2-8 ml o. i.m.; 15-30 ml r. as basal anaesth.	4 ml o. r. up to 3 × p.d.					5	10	5	10
Penicillin G Procaine. See Procaine Benzylpenicillin										
Pentaquine Phosphate* (Pentaquini Phosphas)			0.02	0.1	—	—				
Pentetrazole. See Leptazol										
Pentobarbitone Sodium (Pentobarbitalum sol.)	0.1-0.2	0.1 1-2 × p.d.; 0.2 i.v.					0.1	0.2		
Pentothal. See Thiopentone										
Pethidine HCl (Pethidinum HCl)	0.025-0.1 o. s.c. i.m.; 0.025-0.05 i.v.	0.1 o. parent. every 4 hours	0.05-0.1 o. s.c. i.m.	0.15-0.2 o. s.c. i.m.	—	—	0.15	0.6		

* See footnote on page 371.

[illegible]

alk. B.P. B.P.C. c.d. D.A.B. div. emet.	alkaloids BRITISH PHARMACOPOEIA 1953 BRITISH PHARMACEUTICAL CODEX 1954 controlling dose DEUTSCHES ARZNEIBUCH 6 divided dose emet. dose	gtt. i.d. i.m. i.v. I.U. m.d. mg	drops initial dose intramuscular intravenous international units maintenance dose milligram	Usual Doses in grams (unless otherwise stated)					Maximal Doses in grams (unless otherwise stated)				
				B.P. or B.P.C.	U.S.P.	P.I., P.G., etc.			P.I.	P.H.			D.A.B.
						oral unless otherwise stated	single	per day		oral unless otherwise stated	single	per day	
Potassium Bromide (Kalii Bromidum)	0.3-1.2	—	1	3	2	6	—	—	—	—	—	—	
Potassium Chlorate (Kalium chloricum)	0.3-0.6	—	0.5	1	—	—	1	3	—	—	—	—	
Potassium Chlorate Lozenges (Pastili Kalii Chlorici) (0.1 g KClO ₃)	—	—	—	—	—	—	No X	No XXX	—	—	—	—	
Potassium Iodide (Kalii Iodidum)	0.3-2, 0.03-0.06 (thyrotoxicosis)	0.3 up to 4 × p.d.	0.5	up to 5	2	6	—	—	—	—	—	—	
Primaquine*	—	15 mg p.d. for 14 days	0.01-0.03	0.01-0.03	—	—	—	—	—	—	—	—	
Procaine Benzylpenicillin (Procaine Benzylpenicillinum)	0.5-1 × 10 ⁶ U. p.d. i.m.	300,000 U i.m. 1-2 × p.d.	300,000 up to 1.2 × 10 ⁶ I.U. i.m.	300,000 up to 1.2 × 10 ⁶ I.U. i.m.	—	—	—	—	—	—	—	—	
Procaine HCl (Procainum HCl)	—	As 1-2% soln. s.c.; intraspi- nal: up to 150 mg as 1-5% soln.	—	—	—	—	0.2	0.6	—	—	—	—	
Procaine Nitrate (Procainum Nitricum)	—	—	—	—	—	—	—	—	—	—	—	—	
Progesterone (Progesteronum)	0.005-0.02 p.d. i.m.	0.01 s.l. up to 4 × p.d.; 0.025 i.m.	0.002-0.01 i.m.	up to 0.02 i.m.	—	—	—	—	—	—	—	—	
Proguanil HCl (Proguanilum HCl)	0.1-0.4 p.d.	—	0.05	0.4	—	—	—	—	—	—	—	—	

Proanthazine HCl (Promethazine HCl)	0.025-0.075 p.d.	0.025; 0.05 i.m.	0.05-0.075	0.05 i.m.	0.10 i.m.				
Propylthiouracil (Propylthiouracilum)	0.2-0.6 p.d. c.d.; 0.05-0.2 p.d. m.d.	0.1 every 8 hours	0.05-0.10	0.10-0.20	0.25	0.50	—	—	—
Pulvis Strychni. See Nux Vomica, Powdered									
Quinaetine. See Mepacrine									
Quinine Sulphate (Quinidini Sulfas)	0.06-0.3	0.2 up to 6 N p.d.	0.2	up to 2	0.5	2	0.3	1.5	
Quinine Dihydrochloride (Quinini Dihydrochloridum)	0.3-0.6					2	0.5	2	
Quinine Hydrochloride (Quinini Hydrochloridum)	0.3-0.6	0.6 i.v.	0.25; 0.2 i.m.	0.5-0.75; 0.5 i.m.	0.5 o. i.m.	2 o. i.m.	0.5	2	
Quinine Sulphate (Quinini Sulfas)	0.3-0.6	1 p.d. for 2 days, then 0.6 p.d. for 5 days	0.25	up to 1.2	0.5	2	0.5	2	
Resorcinol (Resorcinum)	—	—	—	—	—	—	0.5	3	
Riboflavin, Vitamin B ₂ (Riboflavinum)	1-4 mg p.d. prophyl. 5-10 mg p.d. therap.	3 mg p.d. o. s.c. prophyl.; 5 mg p.d. o. s.c. therap.	0.01; 0.002 s.c.	up to 0.03 o. s.c.	—	—	—	—	
Sabina (Herba Sabinae)	—	—	0.5	1.5	—	—	0.5	1	
Salol (Salolium)	—	—	—	—	—	—	2	6	
Salophen. See Acetyl- <i>p</i> -aminophenyl Salicylate									
Santonin (Santoninum)	0.06-0.2		0.05	0.1	0.1	0.3	0.1	0.3	0.3
Santonin Tablets (Pastilli Santonini)	—	—	—	—	—	—	No IV	No XII	
Scopolamine. See Hyoscine									

Abbreviations:

alk.	alkaloids	ggt.	drops	minimum	r.	rectal
B.P.	BRITISH PHARMACOPOEIA 1953	i.d.	initial dose	millilitre or ccm	s.c.	subcutaneous
B.P.C.	BRITISH PHARMACEUTICAL CODEX 1954	i.m.	intramuscular	oral	s.d.	single dose
c.d.	controlling dose	i.v.	intravenous	per day	s.l.	sublingual
D.A.B.	DEUTSCHES ARZNEIBUCH 6	I.U.	international units	PHARMACOPOEA GALICA VII	tot.	total
div.	divided dose	m.d.	maintenance dose	PHARMACOPOEA HELVETICA V	U.	units
emet.	emetic dose	mg	milligram	PHARMACOPOEA INTERNATIONALIS	U.S.P.	UNITED STATES PHARMACOPOEIA XV

	Usual Doses			Maximal Doses		
	in grams (unless otherwise stated)			in grams (unless otherwise stated)		
	B.P. or B.P.C.	U.S.P.	P.I., P.G., etc.	P.I.	P.H.	D.A.B.
	oral unless otherwise stated			oral unless otherwise stated		
	single	single	single	single	per day	single
Secale Cornutum. See Ergot						
Semen Strychnis. See Nux Vomica						
Silver Nitrate (Argentum Nitricum)	—	—	0.01	0.03	0.1	0.03 0.1
Silver Protein (Argentum Proteinicum)	—	—	0.05	—	—	—
Sodium Acetylarsanilate (Natrium Acetylarsanilicum)			0.05 o. s.c.	0.1 o. s.c.	0.25	0.2
Sodium Antimonyl tartrate. See Antimony Sodium Tartrate						
Sodium Arseniate (Natrium Arsenicum)			0.001	0.01	0.02	
Sodium Arseniate Solution (PEARSON'S Solution) (Natrium Arsenicum Solutum)				5	10	
Sodium Bromide (Natrii Bromidum)	0.3 3 × p.d.	0.5-1	3	2	—	—
Sodium Cacodylate (Natrium Cacodylicum)		0.05 s.c.	0.1 s.c.	0.1; 0.2 s.c.	0.3; 0.6 s.c.	—
Sodium Citrate (Natrii Citras)	1-4	1 4 × p.d.	1; 0.02/kg i.v.	—	—	—

	0.3-2; 0.03-0.06 (thyrotoxicosis)	0.3 3 × p.d.	0.5	2	2	2	6	—	—	—	—	—
Sodium Iodide (Natrii Iodidum)												
Sodium Nitrite (Natrium Nitrosum)	0.03-0.12; 0.3 i.v. (cyanide poisoning)	0.03 3 × p.d.	0.03-0.05	0.10-0.20	0.10	0.30	0.1	0.3	0.3	1.0		
Sodium Salicylate (Natrii Salicylas)	0.6-2	0.6 every 2-4 hours	1; 0.1-1 i.v.	up to 10; 1-3 i.v.	2	12	—	—	—	—		
Sparteine Sulphate (Sparteinum Sulfuricum)			0.05-0.1	0.1-0.25			0.2	0.6				
Spirit of Nitrous Ether (1.25-2.5%) (Spiritus Aetheris Nitrosi)	1-4 ml		5-20 gtt	—			1	5	—	—		
Squill (Bulbus Scillae)	0.06-0.2		0.1	0.5	0.5	1	0.5	1.5	—	—		
Squill Extract, Dry (1 g = 1 g Squill) (Extractum Scillae)							0.3	1				
Squill Tincture ... (1 g = 0.1 g Squill) (Tinctura Scillae)	0.3-2 ml		0.25-1 up to 2	3-5	2	8	2	6	—	—		
Stibii et Kalii Tartras. See Antimony Potassium Tartrate												
Stibii et Natrii Tartras. See Antimony Sodium Tartrate												
Stibophen (Stbophenum)	0.1-0.3 i.v.	0.1-0.3 i.m. every 2 days	0.1-0.3 i.m. i.v.	—	—	—	—	—	—	—		
Stilboestrol (Diethylstilboestrolum)	0.0001-0.005 p.d.	0.0005 p.d.	0.001	up to 0.005	—	—	—	—	—	—		
Stramonium (min. 0.2% alk.) (Stramonii Herba)	—		—	—	—	—	0.3	1	0.2	0.6		
Stramonium, Powdered... (0.25% alk.) (Pulvis Stramonii Herbae)	0.06 3 × p.d. rising to 2 p.d. or more (parkinson- ism)		0.1	—	0.25	1						
Stramonium Seed .. (min. 0.25% alk.) (Semen Stramonii)							0.2	0.6				
Stramonium Tincture .. (0.05% alk.) (Tinctura Stramonii)	0.6-2 ml; 2-16 ml (parkinsonism)		0.30-1	1.50-3	2	8	1	3	—	—		

Abbreviations:

alk.	alkaloids	ggt	drops	min.	minimum	r.	rectal
B.P.	BRITISH PHARMACOPOEIA 1953	i.d.	initial dose	ml	millilitre or ccm	s.c.	subcutaneous
B.P.C.	BRITISH PHARMACEUTICAL CODEX 1954	i.m.	intramuscular	o.	oral	s.d.	single dose
c.d.	controlling dose	i.v.	intravenous	p.d.	per day	s.l.	sublingual
D.A.B.	DEUTSCHES ARZNEIBUCH 6	I.U.	international units	P.G.	PHARMACOPOEA GALLICA VII	tot.	total
div.	divided dose	m.d.	maintenance dose	P.H.	PHARMACOPOEA HELVETICA V	U.	units
emet.	emetic dose	mg	milligram	P.I.	PHARMACOPOEA INTERNATIONALIS	U.S.P.	UNITED STATES PHARMACOPEIA XV

	Usual Doses in grams (unless otherwise stated)				Maximal Doses in grams (unless otherwise stated)			
	B.P. or B.P.C.	U.S.P.	P.I., P.G., etc.		P.I.		P.H.	
	oral unless otherwise stated			oral unless otherwise stated		oral or parenteral unless otherwise stated		
	single	single	single	per day	single	per day	single	per day
	single	single	single	per day	single	per day	single	per day
Streptomycin HCl, H ₂ SO ₄ , etc. (Streptomycinum HCl, H ₂ SO ₄ , etc.)	1 p.d. (base) s.c.	0.5 p.d. (base) i.m.	0.50-1 i.m.*	0.50-2 i.m.	—	—	—	—
Strophanthin-G. See Ouabain								
Strophanthin-K (40% Ouabain activity) (Strophanthinum-K)	0.25-1 mg i.m. i.v.							
Strychnine Nitrate (Strychnini Nitras)			0.001- 0.002; 0.001- 0.002 s.c.	0.003- 0.005; 0.002- 0.004 s.c.	0.006	0.018	0.01	0.005
Succinylsulphathiazole (Succinylsulfathiazolum)	3-6	2 every 4 hrs.	3-6	6-10 up to 25	—	—	—	—
Sulphadiazine (Sulfadiazinum)	3 i.d.; 1-1.5 m.d. every 4 hrs.	4 i.d.; 1 m.d. every 4 hours	2-3	6-12	—	—	—	—
Sulphadiazine Sodium (Sulfadiazinum Natrium)	1-2 i.v.	4 i.v.	2 i.v.	6-8 i.v.	—	—	—	—
Sulphadimidine (Sulfadimidina)	3 i.d.; 1-1.5 m.d. every 6 hrs.							
Sulphadimidine Sodium (Sulfadimidina Sodium)	1-2 i.v.							
Sulphaguanidine (Sulfaguanidinum)	3-6		2-3	6-8 up to 16	—	—	—	—

Sulphanilamide (Sulfanilamidum)	3 i.d.; 1-1.5 m.d. every 4 hrs.		2-3	6-12	—	—	1	5	
Sulpharsphenamine (Sulfarsphenaminum)	0.1-0.6 s.c. i.m.		0.1-0.6 s.c. i.m.	0.1-0.6 s.c. i.m.	—	—	—	—	
Sulphathiazole (Sulfathiazolum)	3 i.d.; 1-1.5 m.d. every 4 hrs.		2-3	5-12	—	—	—	—	
Sulphathiazole Sodium (Sulfathiazolum Natrium)	1-2 i.v.		1-3 i.v.	3-9 i.v.	—	—	—	—	
Sulphonah (Sulfonalum)			1	—	—	—	2	4	1 2
Suramin (Suraminum)	1-2 i.v.								
Tartar Emetic (Tartarus Stibiatus). See Antimony Potassium Tartrate									
Terramycin. See Oxytetracyclin									
Testosterone (Testosteronum)	0.1-0.6 tot. (implant)	0.3 (implant); 0.01 p.d. s.l.; 0.025 p.d. i.m.					—	—	
Testosterone Propionate (Testosteroni Propionas)	0.005-0.025 p.d. i.m.	0.025 p.d. i.m.	0.01-0.04 i.m.	0.01-0.04 i.m.	—	—	—	—	
Tetrachloroethylene (Tetrachloroethylenum)	1-3 ml s.d.	3 ml	1-3 ml	1-3 ml	5 ml	5 ml			
Thebaine HCl (Thebainum HCl)							0.05	0.2	
Theobromine (Theobrominum)	0.3-0.6		0.3	up to 3			0.5	3	
Theobromine and Calcium Salicylate (Theobromino-Calcium Salicylicum)			0.5	—			1	6	
Theobromine and Sodium Salicylate (Theobrominum Natrium et Natrii Salicylas)	0.6-1.2		0.5	1.5	1.5	6	1	6	—
Theobromine Sodium and Sodium Acetate (Theobrominum Natrium et Natrii Acetas)			0.25-0.5; 0.25 s.c.	0.75	1	3			

* Intraspinal 0.025-0.10; intrapleural 0.25-0.50.

Abbreviations:

alk. alkaloids
B.P. BRITISH PHARMACOPOEIA 1953
B.P.C. BRITISH PHARMACEUTICAL CODEX 1954
c.d. controlling dose
D.A.B. DEUTSCHES ARZNEIBUCH 6
div. divided dose
emet. emetic dose

r. rectal
s.c. subcutaneous
s.d. single dose
s.l. sublingual
tot. total
U. units
U.S.P. UNITED STATES PHARMACOPOEIA XV

	Usual Doses in grams (unless otherwise stated)					Maximal Doses in grams (unless otherwise stated)				
	B.P. or B.P.C.	U.S.P.	P.I., P.G., etc.		P.I.	P.H.	D.A.B.			
	oral unless otherwise stated									
	single	single	single	per day				single	per day	
Theophylline (Theophyllinum)	0.06-0.2 o. r.	—	0.1-0.4 o. r.	0.2-0.5 o. r.	0.5 o. r.	1 o. r.	0.5	1.5	1.5	
Theophylline Sodium and Sodium Acetate (Theophyllinum Natricum et Natrii Acetas)			0.1-0.5	0.5	0.5	1.5	0.75	2.0		
Thiamine. See Aneurine										
Thiopentone Sodium (Thiopentalum Natricum cum Natrii Carbonate)	0.1-0.5 i.v.; 0.04/kg (max. 2) r.	2-3 ml 2.5 % soln. i.v. re- peated as ne- cessary	0.25-0.5 i.v.	0.25-0.5 i.v.	—	—	0.25	—	—	
Thymol (Thymolum)	0.03-0.12; 1-2 as anthelmintic						1	5	—	
Thyroid (Glandulae Thyreoideae Siccatae)	0.03-0.24 p.d.	0.06 p.d.	0.01-0.10	0.05-0.10 up to 0.25	0.25	0.50	—	0.5	1	
Thyroxine Sodium (L-Thyroxinum Sodium)	0.1-0.5 mg									
Tribromoethyl Alcohol..... (Tribromaethanololum)	0.075-0.1/kg r. (as basal anaesth.); max. 10 men, 8 women	0.06-0.08/kg r.; max. 10 men, 8 women	0.06-0.09 kg r.; max. 8-10		—	—				
Tromexan (GEIGY). See Ethyl Biscoum- acetate										
Tryparsamide (Tryparsamidum)	1-2 s.c. i.m. i.v.	3 i.v. weekly	1-3 per week i.v.	—	—	—				

Tuberculin, Old (Tuberculinum Pristinum)	Diagnostic: 1, 10 or 100 U. in 0.1 ml, intracut.	—	0.00001– 0.001 ml intracut.	—	—	—	—	—	—
Unguentum Hydrargyri Cin. See Mercury Ointment, Grey									
Urethane (Urethanum)	1–2	3–4	0.50–1	3 p.d.	0.00001– 0.001 ml intracut.	—	—	—	—
Vasopressin Injection (Injectio Vasopressini)	5–15 U. s.c. i.m.	15 U. s.c. i.m.	5 U. s.c. i.m.	1 ml. i.m. (= 20 U.)	0.00001– 0.001 ml intracut.	—	—	—	—
Viola Crystallina. See Crystal Violet									
Vitamin A	2500–25,000 U. p.d.	—	—	5000 U. p.d. prophyl.; 25,000 U. therap.	0.00001– 0.001 ml intracut.	—	—	—	—
Vitamin B ₁ . See Aneurine HCl									
Vitamin B ₂ . See Riboflavine									
Vitamin B ₁₂ . See Cyanocobalamin									
Vitamin C. See Ascorbic Acid									
Vitamin D ₃ . See Calciferol									
Yohimbine HCl (Yohimbinum HCl)		up to 0.015	0.005		0.00001– 0.001 ml intracut.	—	0.02; 0.01 s.c.	0.06	0.1
Zinc Sulphate (Zincum Sulfuricum)	0.6–2 emet.	—	—	—	0.00001– 0.001 ml intracut.	—	1	1	—

From the University Pediatric Clinic, Zurich (Director, Prof. G. FANCONI) and the Cantonal Nursery (Director, Prof. H. WILLI) of the University Gynaecological Clinic, Zurich (Director, Prof. E. HELD)

by Dr. med. R. FREY

It is customary to derive the posology of drugs in the treatment of children by calculation from the doses appropriate to adults. The various formulae which are in use for this purpose yield widely differing results. In common use, for example, are HAHN's table (children's doses as percentages of adult doses), YOUNG's rule:

$$\text{children's dose} = \text{adult dose} \times \frac{\text{age (in years)}}{\text{age} + 12},$$

CLARK's rule:

$$\text{children's dose} = \text{adult dose} \times \frac{\text{body weight in pounds}}{150},$$

and the simple rule of thumb (AUGSBURGER):

dose from first year of life on
 $= (4 \times \text{age in years} + 20)\%$ of adult dose,
 derived from CLARK's formula for posology according to body surface area:

$$\text{children's dose} = \text{adult dose} \times \frac{\text{child's weight}^{2/3}}{\text{adult weight}^{2/3}}$$

Most of these formulae are based on the *age of the child*, the most readily accessible measurement for the practitioner at the sick-bed. More exact is posology based on *body weight*, although this suffers from the disadvantages that the use of the same value (g/kg) both for infants and for older children leads to anomalous results and that the exact weight of the child is often not known with certainty. A rough estimate of the weight will not give results any more accurate than those arrived at from the age (in posology according to age, obviously the stage of development and the constitution of the child must be taken into account). The most accurate and simple method would be posology according to the *body surface*, where a single value (g/m²) for each drug is valid from infancy to old age; the body surface can be obtained quite simply from the weight and height by means of a nomogram (see the enclosure in the pocket inside the back cover of these *Tables*). These two measurements are also often not known with certainty, however, so that the practitioner is again reduced to rough estimation and inaccurate results. This method too is therefore not always practicable where rapid calculation of the dosage for a child is called for.

Since this dosage table is intended for the use of the general practitioner, the doses are in the main based on age and only in the case of certain groups of drugs on weight; doses are given for the usual three age groups, infancy/early childhood/midchildhood, the lower values

being in each case appropriate to the younger children in the group. The limits of variation of the intensity of treatment (weakest dose to strongest dose) are indicated roughly by the number of single doses per day. The age group early infancy (0-3 months) has not been included since the majority of drugs are only rarely administered during this period. The values given for dosage according to body surface (g/m²) have been calculated both from the usual adult doses and from the children's doses given; the data given in the columns "Number of single doses per day" and "Remarks" apply equally to the posology according to body surface and according to age. For convenience the average values for "normal weight" and body surface for the three age groups have been included in the column headings (for more exact data on weight, see the tables on pages 257-266, for calculation of body surface, see the nomogram in the pocket inside the back cover). Weights are given as a rule in grams and only exceptionally, where this is usual (*antibiotics*), in milligrams.

The table includes only those drugs of importance to the general practitioner. Substances which can be used only under clinical conditions have been excluded. The table is furthermore restricted to drugs the exact dosage of which is of importance. In the main the substances listed are accepted pharmacopoeial drugs and the only specialties included are those which are in frequent use. Obviously this tabular summary can offer only a limited selection both as regards the preparations listed and their modes of application and has many unavoidable gaps.

The posology of drugs for children, as for adults, will vary within certain limits according to the experience of each individual practitioner. This results in considerable differences, just as the values given in the literature in respect of a particular drug also show very marked differences. Apart from the particular indications given, such a tabular summary can therefore only show the limits inside which the practitioner can vary the dose according to the nature and severity of the disease, the constitution and development of the child, and his own personal experience. The doses given are to be regarded as the usual effective doses and are neither minimal nor maximal doses.

In general it should be noted that young children and infants exhibit a relatively low sensitivity to soporifics and narcotics, as also to adrenaline, atropine, quinine, iodine, mercury, castor oil, sulphonamides, thyroid preparations. They are especially sensitive to antipyretics (acetylsalicylic acid, amidopyrine) and to stimulants (camphor, caffeine, nikethamide, etc.).

In infancy, cocaine and morphine and their derivatives (except codeine) are not well tolerated.

Weights are in grams unless otherwise stated.
N.B. In using this table it is important that special attention be paid to the data given in the columns headed "Number of single doses per day" and "Remarks", as well as to the introductory remarks on page 401.

Abbreviations:

amp. = ampule(s)
B.P. = British Pharmacopoeia
B.P.C. = British Pharmaceutical Codex
drag. = dragée(s)
ext. = external
ggt. = drops
inh. = inhalant
i.m. = intramuscular
i.v. = intravenous
I.U. = international units
max. = maximum
mg = milligram(s)
min. = minimum
ml = millilitre(s)
o. = oral
p.d. = per day
p.inf. = pro infantum
P.H. = Pharmacopoea Helvetica
P.I. = Pharmacopoea Internationalis
r. = rectal
s.c. = subcutaneous
soln. = solution
supp. = suppository(ies)
tbl. = tablet(s)
U. = unit(s)
U.S.P. = United States Pharmacopoeia
µg = microgram = 0.001 mg

	Single dose (unless otherwise stated) for:				Number of single doses per day	Ad-min-istra-tion	Commercial form, composition, content	Remarks
	3-12 months 5-10 kg 0.35-0.40 m²	3-5 years 15-20 kg 0.6-0.75 m²	6-12 years 20-40 kg 0.85-1.3 m²	1 m² body surface				
Acedicon (BOEHRINGER) Acetyldemethylodihydrothebaine hydrochloride	—	0.0005-0.001	0.001-0.0025	0.0015	1-3	o.	tbl. 0.005	With sugar in water before meals; larger doses only in case of severe coughing (evenings).
Acetophenetidin U.S.P. See Phenacetin								
Acetylcholine chloride	—	0.02-0.05	0.05	0.05	daily	s.c.	amp. 0.02 and 0.2 supp. 0.3	
Acetylsalicylic Acid B. P.	0.05-0.1	0.1-0.15	0.2-0.3	0.25- (0.5)	2-3	o.	tbl. 0.3	In hot water with sugar (sparingly soluble); best in small portions; not even-ings (danger of collapse!).
ACTH, Corticotropin Adrenocorticotrophic hormone of anterior pituitary	from 6 months 5-10 mg	10-40 mg	40-60-80 mg	25- 50 mg	daily in 4-6 portions	s.c. i.m.		In allergic reactions usually for 5 days at most. In other indications higher doses according to nature and severity of illness! Add potassium chloride ½-3 g p.d., low-salt diet, vitamins B and C, antibiotics.
Adrenaline* Hydrochloride Solution B. P. Epinephrine U.S.P.	0.2-0.3 ml	0.3-0.5 ml	0.5-0.75 ml	0.5 ml	one or more times p.d.	s.c. i.m.	1‰ soln. 0.001 per ml	In emergency intracardial up to 1 ml of soln. Maximum hypodermic dose for adults: single 0.5 ml, per day 2.0 ml.
Allonal (ROCHE)	½ tbl.	¼-1 tbl.	1-1½ tbl.		1-2-(3)	o.	tbl. 0.16: allyliso-propylbarbituric acid 0.06, amidopyrine 0.1	As analgesic, evenings as soporific.
Aloxyn (HOMMEL) . See Nyxolan (HOMMEL)								

Amidopyrine B.P.C. Dimethylaminoantipyrin Dimethylaminophenyldimethyl- pyrazolone Dipyrin	0.02-0.05	0.1-0.15	0.1-0.2	0.15- (0.3)	1-2-(3)	o.	tbl. 0.1 and 0.3	As antipyretic the daily dose is best administered in smaller doses at more frequent intervals. In polyarthritis larger doses ($\times 2-3$). Caution, children are sometimes hypersensitive! Leucocyte control (agranulocytosis)!
Aminophylline B.P.	0.025 $\frac{1}{4}$ supp.	0.05 $\frac{1}{2}$ supp.	0.10 1 supp.	0.15 0.3	1-3	o. i.m. r.	tbl. 0.1; amp. 2.4% soln. (1 ml = 0.024); supp. 0.36. Theophylline ca. 80%, ethylene- diamine ca. 13%	On 2 days in the week. Readily soluble in water.
Ammonium Bromide B.P.C.	0.1-0.25	0.3-0.5	0.5-1.0	0.75	2-3	o.	ca. 80% bromine	In mixtures with Liquorice Extract.
Ammonium Chloride B.P.	0.125-0.25	0.3-0.5	0.5-0.8	1.0	daily	o.	In 0.5-2% soln. according to age with 2% Liquorice Extract	In water or milk after meals. In spasmo- philia in 10% soln., up to 0.6 per kg body weight in milk (can irritate the gastric mucosa).
Ammonium Chloride Mixture Mixtura Solvens P.H.	0.5-2% ammonium chloride according to age with 1% Liquorice Extract				see remarks	o.		Mixture containing 5-10 ml of the appropriate soln. 4-5 times p.d.
Amyl Nitrite B. P.	1-3 gtt.	1-3 gtt.	1-4 gtt.			inh.	1.0 = 68 standard drops	
Aneurine Hydrochloride B. P. See Vitamin B ₁								
Antihistamines	in general 0.5-1 mg/kg body weight			0.03	3-4-(5)	o. s.c.		Start with small doses and increase cautiously. Antidote: histamine acid phosphate 0.1 mg/kg body weight s.c.
Antipyrene ** See Phenazone								
Apomorphine Hydrochloride B.P. ...	—	0.0025	0.004	0.004	1	s.c.	In 0.5% soln.	Caution! Danger of collapse.

* In USA the name *Adrenalin* is a registered trademark (PARKE, DAVIS).

** In Germany the name *Antipyrin* is a registered trademark (HOECHST).

Weights are in grams unless otherwise stated.
N.B. In using this table it is important that special attention be paid to the data given in the columns headed "Number of single doses per day" and "Remarks", as well as to the introductory remarks on page 401.

Abbreviations:

amp. = ampule(s)
B.P. = British Pharmacopoeia
B.P.C. = British Pharmaceutical Codex
drag. = dragée(s)
ext. = external
gtt. = drops
inh. = inhalant
i.m. = intramuscular
i.v. = intravenous
I.U. = international units
max. = maximum
mg = milligram(s)
min. = minimum
ml = millilitre(s)
o. = oral
p.d. = per day
p.inf. = pro infantum
P.H. = Pharmacopoea Helvetica
P.I. = Pharmacopoea Internationalis
r. = rectal
s.c. = subcutaneous
soln. = solution
supp. = suppository(ies)
tbl. = tablet(s)
U. = unit(s)
U.S.P. = United States Pharmacopoeia
µg = microgram = 0.001 mg

Posology in Infancy and Childhood (continued)

	Single dose (unless otherwise stated) for:				Number of single doses per day	Ad-min-istration	Commercial form, composition, content	Remarks
	3-12 months 5-10 kg 0.35-0.40 m ²	3-5 years 15-20 kg 0.6-0.75 m ²	6-12 years 20-40 kg 0.85-1.3 m ²	1 m ² body surface				
Arsenical Solution B.P. Fowler's Solution	1 gtt. up to 3 gtt. of the solution diluted with 3 parts Peppermint Water	2 gtt. up to 9 gtt.	5 gtt. up to 18 gtt.		3	o.	1.0% arsenic trioxide (1.0 = 38 standard drops)	Use diluted with 3 parts Peppermint Water (reduced dosage error); increase from smallest to largest dose during 2-3 weeks, then reduce again.
Ascorbic Acid B. P. See Vitamin C								
Aspidium Oleoresin U.S.P. See Male Fern Extract								
Atebrin. See Mepacrine Hydrochloride								
Atropine Methonitrate B.P.C.	0.0002-0.0004	0.0004-0.0006	0.0006-(0.001)	0.0008	3	o.	tbl. 0.001	Administer in 1% soln. Less toxic and less active than atropine.
Atropine Sulphate B.P.	0.0001-0.0002	0.0002-0.0003	0.0003-0.0005	0.0004	1-2-3	o.	In fresh 1% aqueous soln. (limited stability) (1 ml = 20 drops = 0.001)	Start with the lower dose and increase cautiously each day. If reddening of face occurs, no further increase.
Aureomycin Hydrochloride B.P.	In general 25 mg/kg body weight in mild and 25-40 mg/kg in severe infections p.d. in 4-6 doses						Capsules with 50 or 250 mg. Spersoids (LEDERLE): powder containing 50 mg per teaspoonful (3 g)	Always give additionally vitamin B complex. Disturbance of bacterial flora, danger of moniliasis! Only in emergency i.v., half dose. Not to be combined with penicillin.
Barbitone B. P. Diethylbarbituric acid Barbitalum	—	0.1-0.2	0.25-0.3	0.25	1	o.	tbl. 0.5	½ hour before bed dissolved in a hot drink.
Barbitone Sodium B. P.	—	0.1-0.2	0.25-0.3	0.25	1	o.	tbl. 0.5	Readily soluble in water.

Belladenal (SANDOZ)	—	1/4-1/3 tbl. 1/2 supp.	1/2 tbl. 1 supp.		* daily in 4-6 parts	o. r.	tbl. with 0.00025 Bellafoleinand0.05 phenobarbitone; supp. with 0.0005 Bellafoleline and 0.1 phenobarbitone	*Starting with the daily dose, increase cautiously to the effective dose (up to × 3). Cave hypersensitivity to atropine!
Belladonna Extract	0.002-0.003	0.003-0.005	0.01-0.03	0.015	2-3	o.r.		In mixture or as suppository.
Bellafoleline (SANDOZ)	1-2 gtt. — —	2-5 gtt. 1/2 tbl. 1/2 supp.	5-10 gtt. 1 tbl. 1 supp.	0.00025	1-2 1-2 1-2	o. o. r.	0.5% soln. (10 ggt. = 0.00025); tbl. 0.00025 corr. to ca. 0.0005 atro- pine sulphate; supp. 0.0005	Caution!
Bellergal (SANDOZ)	1/2 drag.	1/2-1 drag.	1-2 drag.		1-2	o.	1 drag. contains 0.0001 Bellafoleline, 0.0003 ergotamine tartrate, 0.02 phenobarbitone	Caution!
Benzylpenicillin B. P.				800,000 U.		i.m. o.	Lozenges contain- ing 1000 U.	Relatively high dosage in infancy! Not to be combined with aureomycin or chloramphenicol. Acts synergistically with sulphonamides and streptomycin. Oral dosage same as i.m.
Borax B.P.								
Borax Sodium borate								
Bromoform B.P.C.								
Bromoform B.P.C.								
Caffeine and Sodium Benzoate B.P.C. (or Caffeine and Sodium Salicylate P.H.)	0.02-0.05	0.05-0.1	0.1-0.2	0.15	2-3	o. s.c.	1.0 = 41 standard drops ca. 47% caffeine; s.c. in 10-20% soln.	Colourless. Readily decomposed; if red in colour do not use! Increase from lower to higher dose in course of 1 week. Ad- minister in syrup. With syrup in water, 1 cup black coffee contains ca. 0.05-0.1 caffeine. In emer- gency also s.c. (painful).
Calcibronat (SANDOZ)	1 knife- point —	1/2 dess. spoonful 1/2 tbl.	1 dess. spoonful 1 tbl.		1-2-(3)	o.	1 dess. spoon granules = 3.0 = 1 efferv. tbl. 15% Br, 7.5% Ca	In water. In infancy administer for a short time only.
Calciferol U.S.P. See Vitamin D₂								
Calcium bromide, anhydrous	0.1-0.3	0.5-1.0	1.0-1.5	1.0	3	o.	In 10% soln.	With plenty of syrup and a few drops Liq. Ammonii anisati in water. In infancy ad- minister for a short time only.

Weights are in grams unless otherwise stated.
N.B. In using this table it is important that special attention be paid to the data given in the columns headed "Number of single doses per day" and "Remarks", as well as to the introductory remarks on page 401.

Abbreviations:

amp. = ampule(s)
B.P. = British Pharmacopoeia
B.P.C. = British Pharmaceutical Codex
drag. = dragée(s)
ext. = external
gtt. = drops
inh. = inhalant
i.m. = intramuscular
i.v. = intravenous
I.U. = international units
max. = maximum
mg = milligram(s)
min. = minimum
ml = millilitre(s)
o. = oral
p.d. = per day
p.inf. = pro infantum
P.H. = Pharmacopoea Helvetica
P.I. = Pharmacopoea Internationalis
r. = rectal
s.c. = subcutaneous
soln. = solution
supp. = suppository(ies)
tbl. = tablet(s)
U. = unit(s)
U.S.P. = United States Pharmacopoeia
µg = microgram = 0.001 mg

	Single dose (unless otherwise stated) for:				Number of single doses per day	Ad-min-istration	Commercial form, composition, content	Remarks
	3-12 months 5-10 kg 0.35-0.40 m²	3-5 years 15-20 kg 0.6-0.75 m²	6-12 years 20-40 kg 0.85-1.3 m²	1 m² body surface				
Calcium Chloride, Hydrated, B.P. (6H₂O)	0.5-1.0	1.0-2.0	1.0-2.0	1.5	2-3	o.	19% Ca. In 10% soln.	Bitter! With syrup or liquorice extract. In spasmophilia up to 6-8% p.d. For babies 2% up to 5% soln. is better, possibly with stomach tube.
Calcium Gluconate B.P. Calcium-SANDOZ	1.0 2 ml	1.5 5 ml	2.0-3.0 10 ml	2.5 10 ml	3 1-2	o. i.m. i.v.	ca. 9% Ca. tbl. 1.5; powder. With Ca lacto- bionate in syrup and amp.	For infants and young children as 10% soln. only (also i.v.).
Calomel. See Mercurous Chloride B.P.								
Camphorated Oil, injectable	½-1 ml	1-2 ml	2 ml	1.5 ml	1-2	i.m.	20% camphor in olive oil	Use sterile amp. ! Cave abscess formation !
Carbachol B.P. Carbamylcholine chloride	— —	¼-½ tbl. —	¼-1 tbl. 0.5 ml	0.001 0.000125	1-3 1-3	o. s.c.	tbl. 0.002; amp. 1 ml = 0.00025	
Carbo adsorbens P.H.	2.0-3.0	3.0-5.0	5.0-10.0	7.5	1-2-(3)	o.	Powder, granules, tbl. 1 teaspoon = ca. 5.0	Fasting, mixed with water or mucilage, followed after 2 hours by saline purge.
Carbromal B.P.C. Bromadalum, Uradal Bromodiethylacetylurea	0.1-0.2	0.2-0.3	0.3-0.5	0.4	1-2-3	o.	tbl. 0.5	As sedative; as soporific the larger dose singly ½ hour before bed in hot water.
Carlsbad Salt	—	1 knife- point	1 tea- spoonful			o.	ca. 55% sodium sulphate	Fasting, in hot water; as purgative 2-3 times larger dose.
Castor Oil B.P. Oleum Ricini	—	10.0-15.0	15.0-20.0		1	o.	1 dess. spoonful = 15	With lemon juice or in warm milk; warm before taking!

Chenopodium Oil B. P. Oil of American Wormseed	—	—	0.3	*	o.	at least 65% ascaridole; 1 = 49 standard drops	*Fasting, in 2 doses during one morning with interval of 1 hour; on a sugar cube with raspberry syrup, or with duodenal tube; 1-2 hours later magnesium sulphate until effective. Not to be repeated before 2-4 weeks! Preliminary diet: high-carbohydrate, low-fat.
Chiniofon Sodium B.P. Sodium 8-hydroxy-7-iodoquinoline-5-sulphonate	0.05	0.1-0.2	0.3	3*	o. r.	tbl. 0.25 and 0.5 also rectal in 1% soln.	* For 8 days, starting with the smaller dose and increasing (but only up to mild diarrhoea!). In amoebiasis.
Chloral Hydrate B.P.	0.2-0.5	0.5-1.0	1.0-2.0	1	r.		Dissolved in 20-30 ml mucilage or water; possibly repeated once after 2-3 hours. Solutions unstable.
Chloramphenicol B.P. Chloromycetin (PARKE, DAVIS)	In general 25-50 mg/kg body weight orally in 4 portions		800-1000 mg		o.	Capsules with 50 or 250 mg; as palmitate 4 ml = 125 mg	Always give vitamin B complex additionally. Disturbance of bacterial flora, danger of moniliasis! Not to be combined with penicillin. Blood control.
Chlortetracycline. See Aureomycin							
Cibalgin (CIBA)	1-2 gtt. 1/4 tbl. —	5-15 gtt. 1/2 tbl. 1/2 supp. p. inf.	12-30 gtt. 1 tbl. 1 supp. p. inf.	1-2 1-2 1-2	o. o. r.	1 tbl. 0.25 = 30 gtt. = 0.22 amido-pyridine and 0.03 allobarbitone. Supp. p. inf. 0.25	
Cinchona Tincture, Compound Tinct. Cinchonae comp. P.H.	3-5 gtt.	10-15 gtt.	20-30 gtt.	3	o.		With sugar in water before meals; combine with Nux Vomica Tincture.
Codeine Phosphate B.P.	0.001-0.003	0.003-0.01	0.01-0.02	2-3	o.	tbl. 0.025, 0.03 and 0.05	With syrup (<i>not</i> Liq. Ammonii anisati) in 0.25% aqueous soln. after meals. Discontinue when somnolence develops! Caution with infants! Codeine Phosphate Syrup B.P.C. with 0.5% codeine phosphate: 1 teaspoonful = ca. 0.034 codeine phosphate.
Codeine Tablets, Compound, B.P.	— 1/2 supp. p. inf.*	1/4 tbl. 1 supp. p. inf.*	1/2 tbl. 1-2 supp. p. inf.*	1-2 1-2	o. r.	tbl. 0.5 = acetylsalicylic acid 0.25, phenacetin 0.25, codeine phosphate 0.005 plus mineral salts.	*Supp. p. inf. (Treupel) 0.25 have acetylsalicylic acid 0.0625, phenacetin 0.125, codeine phosphate 0.005 plus mineral salts.
Cod-Liver Oil B.P. Oleum Jecoris	5 ml	10 ml	15 ml	2-3	o.	1 ml contains on average 1,000 I.U. vit. A (B.P. min. 600) plus 100 I.U. vit. D (B.P. min. 85)	Where possible use only standardized preparations! Give after meals. After 4-6 weeks 1 week intermission.

Weights are in grams unless otherwise stated.

N.B. In using this table it is important that special attention be paid to the data given in the columns headed "Number of single doses per day" and "Remarks", as well as to the introductory remarks on page 401.

Abbreviations:

- amp. = ampule(s)
B.P. = British Pharmacopoeia
B.P.C. = British Pharmaceutical Codex
drag. = dragée(s)
ext. = external
ggt. = drops
inh. = inhalant
i.m. = intramuscular
i.v. = intravenous
I.U. = international units
max. = maximum
mg = milligram(s)
min. = minimum
ml = millilitre(s)
o. = oral
p.d. = per day
p.inf. = pro infantum
P.H. = Pharmacopoea Helvetica
P.I. = Pharmacopoea Internationalis
r. = rectal
s.c. = subcutaneous
soln. = solution
supp. = suppository(ies)
tbl. = tablet(s)
U. = unit(s)
U.S.P. = United States Pharmacopoeia
μg = microgram = 0.001 mg

	Single dose (unless otherwise stated) for:				Number of single doses per day	Ad-min-istra-tion	Commercial form, composition, content	Remarks
	3-12 months 5-10 kg 0.35-0.40 m ²	3-5 years 15-20 kg 0.6-0.75 m ²	6-12 years 20-40 kg 0.85-1.3 m ²	1 m ² body surface				
Coramine (CIBA). See Nikethamide								
Corticotropin. See ACTH								
Cortisone Acetate B.P.C.	10-20 mg	20-80 mg	80-120 mg	50-150 mg	daily in 4-6 portions	o.	tbl. 25 mg	In allergic reactions; maximum duration usually 5 days. Potassium chloride 1/2-3 p.d. additionally, low-salt diet, antibiotics, vitamins B and C. In other indications other dosage, e.g. in chronic adrenal insufficiency 5/15/20 mg p.d. according to age group.
Crystal Violet B.P. Gentian Violet Methylrosaniline chloride	—	10 mg for each year of life		0.08	* daily	o.		*Duration 8-10 days (anthelmintic); repetition of cure after 8-10 days.
7-Dehydrocholesterol, Activated, U.S.P. See Vitamin D ₃								
Dextrose B.P. Glycosum D-Glucose					s.c. in 5% soln. up to 50-100 ml, i.m. in 10% soln. up to 20-30 ml, i.v. in 20% soln. 5/10/20 ml. For infants 5% soln. for i.m. and i.v. also.			
Diethylbarbituric acid. See Barbitone								
Digilanid (SANDOZ)	Digitalizing dose (0.02 mg/kg): 6-12 gtt. 16-24 gtt. 24-40 gtt. Maintenance dose: ca. 1/5 of digitalizing dose as daily dose			0.0003-0.0006	daily in 4 portions*	o.	Cryst. lanatosides from <i>Digit. lanata</i> . 1 ml soln. = 30 gtt. = 2 drag. = 1 supp. = 0.0005; amp.: 1 ml = 0.0002	* According to condition of patient digitalizing dose should be distributed over 1-1 1/2-2-(3) days, followed by maintenance dose. Cave accumulation! Continuous medical attention.

Digitalis, Prepared , B.P. Digitalis Leaf, Powdered, Standardized, P.I.	Digitalizing dose (30-45 mg/kg): 0.15-0.2 0.3-0.5 0.5-0.8 Maintenance dose: ca. 1/10 of digitalizing dose as daily dose	0.6	daily in 4 portions*	o.	1.0 = 10 I.U. As powder in pills or supp., not as in- fusion	* According to condition of patient digitalizing dose should be distributed over 1-1½-2-(3) days, followed by maintenance dose. Cave accumulation! Continuous medical attention.
Digitoxin B.P.C. Digitalinum cryst.	Digitalizing dose (0.02 mg/kg): 0.0001- 0.0003- 0.0006- 0.0002 0.0005 0.0008 Maintenance dose: ca. 1/10 of digitalizing dose as daily dose	0.0003- 0.0006	daily in 4 portions*	o.	Cryst. glycoside from <i>Digitalis</i> <i>purpurea</i>	* According to condition of patient digitalizing dose should be distributed over 1-1½-2 days, followed by main- tenance dose. Cave accumulation! Con- tinuous medical attention.
Dihydrocodeine bitartrate	— 0.0025-0.005 0.005-0.01	0.006	1-2-3	o.		Stronger action than codeine.
Dihydrocodeinone bitartrate	— 0.001-0.0025 0.0025-0.005	0.003	1-2	o.	tbl. 0.005 and 0.01	After meals in syrup. Infants are hyper- sensitive!
Emetine Hydrochloride B.P.	0.005-0.01 0.015-0.025 0.03	0.03	daily in 3 portions	i.m.		In amoebiasis for 5 days, followed by chiniofon sodium (q.v.) or acetarsol (e.g. 14-day cure according to age: 0.125/0.25/ 0.25-0.5 p.d. oral). Give caffeine with emetine injections.
Ephedrine Hydrochloride B.P. (-)-2-Methylamino-1-phenylpropan- 1-ol hydrochloride	0.005-0.01 0.025 0.025-0.05 — 0.3-0.5 ml 0.5-0.75 ml	0.03	1-3 1	o. s.c.	tbl. 0.03 and 0.05, granules 0.01, amp. 1 ml = 0.05	Even smaller doses at first! If ineffective repeat once after ½-1 hour.
Epinephrine . See Adrenaline						
Ferrous Iodide Syrup B.P.C.	10 gtt. 15-25 gtt. 30-40 gtt.		3	o.	5% ferrous iodide; 1.0 = 16 standard drops	In a little milk before meals.
Filicin Extract . See Male Fern Extract						
Gentian Violet . See Crystal Violet						
D-Glucose . See Dextrose						
Guaiaicol carbonate	0.1 0.3 0.5	0.5	3	o.	tbl. 0.5	As powder in milk or mucilage. Cf. also Potassium Guaiaicolsulphonate.
Hexamine B.P.C. Hexamethylenetetramine Urotropine	0.125 0.125-0.25 0.25-0.5	0.35	3	o.	tbl. 0.3	In aqueous soln.; only effective in acid urine.
Hexeton (BAYER)	0.1-0.2 ml 0.2-0.5 ml 0.5-1.0 ml		1-2	i.m.	amp. 10% soln.	Only i.m.! Not i.v.!
Methylisopropylcyclohexenone						

Weights are in grams unless otherwise stated.
N.B. In using this table it is important that special attention be paid to the data given in the columns headed "Number of single doses per day" and "Remarks", as well as to the introductory remarks on page 401.

Abbreviations:
amp. = ampule(s)
B.P. = British Pharmacopoeia
B.P.C. = British Pharmaceutical Codex

drag. = dragée(s)
ext. = external
gtt. = drops
inh. = inhalant
i.m. = intramuscular
i.v. = intravenous

I.U. = international units
max. = maximum
mg = milligram(s)
min. = minimum
ml = millilitre(s)
o. = oral

p.d. = per day
p.inf. = pro infantum
P.H. = Pharmacopoea Helvetica
P.I. = Pharmacopoea Internationalis
r. = rectal
s.c. = subcutaneous

soln. = solution
supp. = suppository(ies)
tbl. = tablet(s)
U. = unit(s)
U.S.P. = United States Pharmacopoeia
µg = microgram = 0.001 mg

	Single dose (unless otherwise stated) for:				Number of single doses per day	Ad-min-istration	Commercial form, composition, content	Remarks
	3-12 months 5-10 kg 0.35-0.40 m²	3-5 years 15-20 kg 0.6-0.75 m²	6-12 years 20-40 kg 0.85-1.3 m²	1 m² body surface				
Hexylresorcinol B.P.C.	—	0.2-0.3	0.4-0.6	0.5	*	o.	Gastric-juice resistant capsules 0.2	* As anthelmintic the whole dose should be taken in the morning in one hour on empty stomach, followed by purgative in the afternoon. Laxative previous evening.
Homatropine Hydrobromide B.P. ...	As mydriatic: 1 gtt. of a 10% soln. in each eye 2-3 times at ¼-hour intervals				1	s.c.		
Hyoscine Hydrobromide B.P. Scopolamine hydrobromide	—	—	0.0001-0.00025	0.0001	3-5	o.	2% alkaloids	As infusion with Liq. Ammonii anisati and syrup; readily decomposes, better therefore to use corresponding dose of Liquid Extract of Ipecacuanha B.P. (2% alkaloids) in a mixture or syrup.
Ipecacuanha B.P.	0.0025-0.0075	0.01-0.025	0.03-0.05	0.03	2-3	o.	10% ipecacuanha, 10% opium; contains 1% morphine and 0.2% ipecacuanha alkaloids	
Ipecacuanha and Opium Powder B.P. Dover's Powder	—	0.03-0.08	0.08-0.15	0.08				
Ipecopan (Sandoz)	1 gtt. of 0.5% soln. for each year of age				3	o.	0.5% soln.: 1 ml = 20 gtt. = 0.00083 ipecacuanha alkaloids and opium alkaloids, corr. to 0.0018 morphine = ca. 0.25 Ipecacuanha and Opium Powder	With sugar in water after meals. Same dosage for Ipedrin (Sandoz): 1 ml = 20 gtt. of the 0.5% soln. contains 0.005 Ipecopan and 0.0075 ephedrine hydrochloride.

Iron, reduced Ferrum reductum P.H.	0.05-0.1	0.1-0.2	0.3-0.5	0.3	3	o.	96% metallic iron	In milk, mucilage, etc.; add lemon juice if necessary. Daily dose for infants 0.3, older children 1.0 or more, of reduced iron; corresponding dosage for other iron preparations. Ferrous salts are more active! Increase slowly; if diarrhoea results, discontinue!
Isoniazid B.P.C. Isonicotinic acid hydrazide	In general 5-10-15 mg/kg body weight p.d. or more in 3-4 portions			0.3-0.6		o. i.m.	tbl. 0.05	After meals. Combine or alternate with streptomycin or PAS.
Isoprenaline Sulphate B.P. Isopropylnoradrenaline sulphate	—	½ tbl.	1-2 tbl.		3	o. inh.	tbl. 0.01; inhalation spray 1% soln.	Tablets should be allowed to dissolve in the mouth.
Kadamysin (ZIMMERMANN)	¼-½ ml	½-¾ ml	1 ml	1.0 ml	* 1-2	s.c.	1 ml contains 0.0008 adrenaline, 0.04 pituitary ex- tract. Also tbl., supp., liq. inhalant	* In asthma attacks dose can be repeated. Also in smaller more frequent doses.
Lactic Acid B.P.	For production of lactic acid milk add 11 gtt. (standard pipette) of a 90% soln. to 100 ml milk (boiled and cooled) with vigorous stirring.							
Lanatoside C	Digitalizing dose (0.00005/kg): 4-8 gtt. Maintenance dose: ca. ½ the digitalizing dose as daily dose	10-15 gtt. 15-30 gtt.		0.0006- 0.0008	daily*	o.	Pure glycoside from <i>Digitalis lanata</i> . 1 ml of soln. = 30 gtt. = 0.001; drag. 0.00025; amp.: 1 ml = 0.0002	* According to condition of patient the digitalizing dose should be spread over 1-1½-2 days, followed by maintenance dose. Action similar to strophanthin, hardly any accumulation.
Leptazol B.P. Pentamethylenetrazole Pentylenetetrazole U.S.P.	0.01-0.025	0.025-0.05	0.05-0.075-0.1	0.06	1-3 1-2	o. s.c. i.m.	10% soln. for in- jection (1 ml = 0.1 = 20 gtt.)	10% soln. can also be used for rectal injection. In infants even the doses stated may induce convulsions!
Liquorice Powder, Compound, B.P. ... Pulvis pectoralis	1 knife- point	½ tea- spoonful	1 tea- spoonful		2-3 at most	o.		As laxative in water with intervals of several hours.
Lobeline Hydrochloride B.P.C.	0.001-0.003	0.005-0.01	0.01	0.0075	*	s.c. i.m.		* Repeat if necessary after 10-15 min. Also for newborn (0.0006, possibly repeated). Not i.v.

Mepacrine Hydrochloride B.P. Quinacrine Hydrochloride U.S.P. Atebrin (Bayer)	0.05-0.1	0.1-0.25	0.25-0.3	0.25	daily in 2-3 portions	o.	With plenty of liquid after meals. Skin pigmentation! Therapeutic in malaria (acts on the schizonts and except in the case of <i>Pl. falciparum</i> also on the gametes; follow up with pamaquine!); the stated doses for 5-7 days. Prophylactic in malaria: for 3-5 years old give 0.1, for 6-12 years 0.4 per week in 2 days in several doses. In lamblasis and trichomonas enteritis the stated doses for 3 days, followed by a repetition of the cure after 14 days. In cutaneous leishmaniasis 1-2 ml of 5-10-15% soln. injected locally once, repeated if necessary after 1 month.
Mercurochrome B.P.C.	In 2% aqueous soln. for painting on burns, etc.						ext. 2% aqueous soln.
Mercurous Chloride B.P. Calomel	0.02	0.03-0.06	0.06-0.15	0.08	*	o.	* Every 2-3 hours with gum arabic in mucilage until effective (2-3-4 doses). Caution! Owing to danger of acrodynia and mercurial poisoning (treat with mercaprol) this drug should be avoided.
Mercurous iodide, yellow	0.005-0.01	0.01-0.02	0.03	0.025	3	o.	In milk after meals.
Mersalyl B.P.	—	1/4-1/2 ml	1/2-1 ml		1	i.m.	As diuretic, preferably administered with 5% theophylline.
Methenamine U.S.P. See Hexamine							
Methoin B.P. Methylphenylethylhydantoin with Phenobarbitone: Hydantal (Sandoz)	0.05 up to 0.1	0.05 up to 0.2 or more	0.05 up to 0.2	0.2	* daily in 2-3 portions	o.	* Individual dosage. Begin with 1/2 tbl. p.d. and increase by 1/2, then 1 tbl. weekly up to effective dose. Blood control! In case of leukopenia, exanthema, fever, swelling of lymph nodes, no further methoin!
Methylphenobarbitone	0.025	0.05-0.1	0.1-0.2	0.1	1-2-3	o.	In warm water with sugar.
Morphine Hydrochloride B.P.	—	0.001-0.003	0.004-0.008	0.004	1-2	o.s.c. r.	Caution occasional hypersensitivity even to small doses!
Myokombin (Boehringer). See remarks under Strophanthin-K							
Neoarsphenamine B.P.	0.005-0.01 per kg body weight (max. 0.015/kg for children)				* daily	i.v.	* 1-2 injections in all (max. 4). In relapsing fever at the start of an attack. Use fresh solns.! In syphilis after penicillin treatment (for dose, see the literature).

Weights are in grams unless otherwise stated.
N.B. In using this table it is important that special attention be paid to the data given in the columns headed "Number of single doses per day" and "Remarks", as well as to the introductory remarks on page 401.

Abbreviations:

amp. = ampule(s)
B.P. = British Pharmacopoeia
B.P.C. = British Pharmaceutical Codex
drag. = dragée(s)
ext. = external
gtt. = drops
inh. = inhalant
i.m. = intramuscular
i.v. = intravenous
I.U. = international units
max. = maximum
mg = milligram(s)
min. = minimum
ml = millilitre(s)
o. = oral
p.d. = per day
p.inf. = pro infantum
P.H. = Pharmacopoea Helvetica
P.I. = Pharmacopoea Internationalis
r. = rectal
s.c. = subcutaneous
soln. = solution
supp. = suppository(ies)
tbl. = tablet(s)
U. = unit(s)
U.S.P. = United States Pharmacopoeia
μg = microgram = 0.001 mg

	Single dose (unless otherwise stated) for:				Number of single doses per day	Ad-min-istration	Commercial form, composition, content	Remarks
	3-12 months 5-10 kg 0.35-0.40 m ²	3-5 years 15-20 kg 0.6-0.75 m ²	6-12 years 20-40 kg 0.85-1.3 m ²	1 m ² body surface				
Neostibosan (BAYER)	0.05-0.1	0.05-0.2	0.1-0.25-0.4	0.2	* daily	i.m.	25 % soln. with ca. 42 % antimony (quinquevalent)	* 8-10 injections in all. In visceral leishmaniasis (kala-azar). For dose in syphilis, see the literature.
Neostigmine Bromide or Methylsulphate B.P. Dimethylcarbamoyloxyphenyltri-methylammonium bromide or methylsulphate	0.2-0.3 ml —	0.3-0.5 ml ¼ tbl.	0.3-1.0 ml ¼-½ tbl.	0.0003	* 3	s.c. o.	amp. 0.5 %, 1 ml = 0.0005 (methylsulphate) tbl. 0.015 (bromide)	*Repeat if necessary. 1 hour after injection enema if necessary.
Nikethamide B.P. Coramine (CIBA) Pyridine-3-carboxydiethylamide	2-5 gtt. 0.1-0.2 ml	5-10 gtt. 0.5 ml	10-20 gtt. 1 ml	0.15 1.0 ml	1 or more 1-3	o. s.c. i.m.	25 % soln., 1 ml = 25 standard drops = 0.25	In water, with drink-shy infants ¼ hour before meals. If necessary larger doses i. v. Larger doses sometimes cause convulsions in infants!
Novocain. See Procaine Hydrochloride								
Nux Vomica Tincture B.P.	2-6 gtt.	8-12 gtt.	12-20 gtt.		3	o.	0.125 % alkaloids	With 3-4 parts Tinct. Cinchonae comp. after meals.
Nyxolan (HOMMEL) Al 8-hydroxyquinoline sulphate	—	1.5	3.0		daily	o.	Granules; syrup (0.4 %, 1 ml = 0.004)	To be taken during 2 periods of 4-6 days with an interval of 10-15 days.
Oleum Jecoris. See Cod-Liver Oil								
Oleum Ricini. See Castor Oil								
Opialum. See Papavaretum								

Opium Extract, Dry, B.P.C.....	—	0.001–0.006	0.015–0.03	0.015	1–2	o. r.	In mixtures or as supp. Caution! Infants are hypersensitive. Stop when sleepiness develops.
Opium Tincture B.P.	—	1–3 gtt.	2–6 gtt.		1–2–3	o.	With sugar in water. Caution! Use only fresh mixtures. See under Opium Extract.
Opium Tincture, Camphorated, B.P. Tinct. Opii benzoica	2–4 gtt.	3–15 gtt.	20–30 gtt.		2–3–(4)	o.	In mixtures or in water. Caution! See under Opium Extract.
Ouabain. See remarks under Strophanthin-K							
Oxophenarsine Hydrochloride B.P. ...	0.01	0.02–0.03		0.02	* daily	i.v.	* With intervals of 1 week. In trypano- some and spirochaete infections.
Oxytetracycline Hydrochloride B.P.C. Terramycin	In general 12.5–25 mg/kg p.d. orally in mild cases and 50 mg/kg p.d. in severe cases, in 4–6 portions			600 mg		o.	Give vitamin B complex additionally.
Pamaquin B.P.	0.001 per kg body weight p.d.			0.03		o.	Children sometimes show toxic symptoms (cyanosis!), when no more should be given. In malaria (no effect on gametes of tropical form) give for 7 days, then 4 days intermission, followed by 4–6 weeks with 3 days treatment alternating with 4 days rest. Incompatible with mepacrine!
Papavaretum B.P.C. Opium Opium Concentratum	From 2–3 years on, as many drops of 2% soln. orally as years of age; s.c. as many 1/10 ml of 2% soln. as years of age. Max. 10 gtt. = 0.6 ml!			0.008	1–2–3 1–2	o. s.c.	With sugar in water. Caution!
Pantopon syrup (Roche)	—	1½ teaspoonful (2.5 ml)	1 teaspoonful (5 ml)		3	o.	
Papaverine Hydrochloride B.P.	0.01–0.02	0.02–0.03	0.04		1–2–3	o. s.c.	Smaller doses s.c. are better!
Papavydrin (Bykopharm, Weil)	½ tbl. p. inf. ½ supp. p. inf.	1 tbl. p. inf. 1 supp. p. inf.			1–3 1–3	o. r.	Papaverine HCl Atropine methonitrate 1 tbl. 0.07 0.00075 1 tbl. p. inf. 0.02 0.0005 1 supp. p. inf. 0.02 0.0003 1 supp. (babies) 0.015 0.0002

Weights are in grams unless otherwise stated.
N.B. In using this table it is important that special attention be paid to the data given in the columns headed "Number of single doses per day" and "Remarks", as well as to the introductory remarks on page 401.

Abbreviations:

amp. = ampule(s)
B.P. = British Pharmacopoeia
B.P.C. = British Pharmaceutical Codex
drag. = dragée(s)
ext. = external
gtt. = drops
inh. = inhalant
i.m. = intramuscular
i.v. = intravenous
I.U. = international units
max. = maximum
mg = milligram(s)
min. = minimum
ml = millilitre(s)
o. = oral
3-12 months
5-10 kg
0.35-0.40 m²
3-5 years
15-20 kg
0.6-0.75 m²
6-12 years
20-40 kg
0.85-1.3 m²
1 m²
body
surface
Number
of single doses
per day
Ad-
min-
istra-
tion
Commercial form,
composition,
content
Remarks
soln. = solution
supp. = suppository(ies)
tbl. = tablet(s)
U. = unit(s)
U.S.P. = United States Pharmacopoeia
µg = microgram = 0.001 mg

	Single dose (unless otherwise stated) for:				Number of single doses per day	Ad- min- istra- tion	Commercial form, composition, content	Remarks
	3-12 months 5-10 kg 0.35-0.40 m ²	3-5 years 15-20 kg 0.6-0.75 m ²	6-12 years 20-40 kg 0.85-1.3 m ²	1 m ² body surface				
PAS, p-Aminosalicylic acid	0.3-0.5 per kg body weight p.d. in 4-6 portions			8.0-10.0				After 5 days treatment 1-2 days intermission. Can also be given rectal in mucilage. May be combined with streptomycin.
Penicillin-G. See Benzylpenicillin								
Pentetrazole. See Leptazol								
Phenacetin B.P.	—	0.1-0.2	0.3-0.5	0.25	2-3	o.	tbl., granules	In liquid (sparingly soluble).
Phenazone B.P.C.	0.05-0.1	0.2-0.3	0.3-0.5	0.3	1-3	o.r.	tbl. 0.5	In water with sugar. Rectal in 10-15 ml mucilage or as suppository.
Antipyrine* Phenyldimethylpyrazolone								
Phenobarbitone B.P.	0.01-0.02	0.02-0.05	0.05-0.1	0.05	1-2	o.		In hot water with sugar.
Phenobarbital Phenylethylbarbituric acid								
Phenobarbitone Sodium B.P.	0.01-0.02 0.25-0.5 ml	0.02-0.05 0.5 ml	0.05-0.1 0.5-1.0 ml	0.05 1 ml!	1-2 See Remarks	o. i.m.	amp. with 20% soln., 1 ml = 0.2	Repeat in emergency. Acts slowly. For convulsions. Maximum hypodermic dose for adults: single 0.2, p. d. 0.4!
Phenytoin Sodium B.P.	0.05	0.05-0.15	0.2-0.3	0.2	daily in 3 portions	o.	tbl. and drag. 0.1 capsules 0.03 and 0.1 according to preparation	With plenty of liquid before meals. Begin with this low dosage and increase weekly up to effective dose. Blood control! Stop if hypersensitivity shown!
Diphenylhydantoin Sodium								
Antisacer comp. p. inf. (WANDER) ...	(1) drag.	1-2 drag.	1-3 drag.		daily	o.	1 drag. contains phenytoin Na 0.05, potassium bromide 0.2, phenobarbitone 0.025, caffeine citrate 0.01, atropine sulphate 0.0002	Start with a small dose and increase weekly until effective. Individual dosage. Blood control and attention to side-effects!

Pholedrine sulphate p-Hydroxyphenylisopropyl- methylaniline	3-4 gtt. —	5-10 gtt. 0.25 ml	10 gtt. 0.25 ml	2-3 1	o. s.c. i.m.	1% soln., 1 ml = 0.01 (for drops); amp. 2% soln., 1 ml = 0.02	s.c. or i.m. only in case of collapse.
Potassium Bromide B.P. Kalium bromatum	0.1-0.25	0.3-0.5	1.0	2-3-(4)	o.		In aqueous soln., preferably in milk. Sodium bromide is better.
Potassium guaiacolsulphonate	0.1-0.2	0.2-0.5	0.5-1.0	3	o.		In mixture with bitter-orange syrup.
Potassium Iodide B.P.	0.025-0.05	0.1-0.2	0.2-0.3	2-3	o.	ca. 76% iodine	In alcoholic soln. in milk. For prophylaxis of goitre much smaller doses, ca. 0.5-1 mg iodide per week. Iodized salt contains 0.5 per 100 kg (in 10 g salt ca. 37 µg iodine). For treatment of goitre 1-5 mg iodide per day.
Procaine Hydrochloride B.P.	1-2 ml	up to 5 ml of 0.5% soln.			s.c.	For children 0.5% soln. only	For infiltration anaesthesia.
Quinacrine. See Mepacrine							
Quinine Hydrochloride B.P.	0.03-0.05-0.1	0.15-0.25	0.3-0.5	1-2-(3)	o. r. i.m.	tbl. 0.3; rectal dose 2-3 times oral. 82% quinine	As antipyretic. In malaria (acts on the schizonts) the stated doses 3 times p.d. until symptoms disappear; then ½ doses for 6-8 weeks. From another source: the stated doses as daily doses until 5 days after disappearance of fever, then in 3-day periods with increasing intervals of 1-5 days; total period of treatment 2 months. Prophylaxis of malaria: the above doses 3 times p.d. on 2 days of the week. Quinine tannate (30% quinine) and quinine ethyl carbonate (81% quinine) are tasteless.
Quinine Sulphate B.P.					o.	83% quinine	Less soluble than quinine hydrochloride; not to be given i.m.!
Riboflavine. See Vitamin B ₂							
Salol B.P.C.	0.05-0.1	0.2-0.3	0.4	3-4	o.	60% salicylic acid, 40% phenol	
Santonin B.P.	0.002-0.005	0.01-0.02	0.03-0.05	see remarks	o.	tbl. 0.025 for children	Twice daily for 2-3 days after meals, with laxative. Not to be repeated for 2-3 weeks. Caution!

* In Germany the name *Antipyrim* is a registered trademark (Hoechst).

Weights are in grams unless otherwise stated.
N.B. In using this table it is important that special attention be paid to the data given in the columns headed "Number of single doses per day" and "Remarks", as well as to the introductory remarks on page 401.

Abbreviations:

amp. = ampule(s)
B.P. = British Pharmacopoeia
B.P.C. = British Pharmaceutical Codex
drag. = dragée(s)
ext. = external
gtt. = drops
inh. = inhaled
i.m. = intramuscular
i.v. = intravenous
I.U. = international units
max. = maximum
mg = milligram(s)
min. = minimum
ml = millilitre(s)
o. = oral
p.d. = per day
p.f. = pro infantum
P.H. = Pharmacopoea Helvetica
P.I. = Pharmacopoea Internationalis
r. = rectal
s.c. = subcutaneous
soln. = solution
supp. = suppository(ies)
tbl. = tablet(s)
U. = unit(s)
U.S.P. = United States Pharmacopoeia
µg = microgram = 0.001 mg

	Single dose (unless otherwise stated) for:				Number of single doses per day	Ad-min-istration	Commercial form, composition, content	Remarks
	3-12 months 5-10 kg 0.35-0.40 m ²	3-5 years 15-20 kg 0.6-0.75 m ²	6-12 years 20-40 kg 0.85-1.3 m ²	1 m ² body surface				
Scopolamine. See Hyoscine								
Sedobrol (Roche)	½ tbl.	½-1 tbl.	1 tbl.		1-2	o.	1 tbl. = 3 ml Sedobrol liquid = 1.1 sodium bromide and 0.1 sodium chloride	With a diet low in salt. Reduce the dose after 1-2 weeks.
Sedormid (Roche)	¼ tbl.	½-1 tbl.	1.tbl.		1	o.	tbl. 0.25	In water before bed.
Allylisopropylacetylurea								
Sodium Bicarbonate B.P.	0.6-1.0	1.0-1.5	2.0-2.5	2.0	3	o.		In water with 1-4 gtt. essence of pepper- mint; in acidosis 1.5% soln. i. v.
Sodium Bromide B.P.	0.1-0.25	0.3-0.5	1.0	0.75	3	o.	ca. 76% bromine	In aqueous soln. with syrup of bitter orange or liquorice extract. In epilepsy up to 4-6-8 times p.d.
Sodium Citrate B.P.	0.5-1.0	1.0-1.5	2.0-2.5	2.0	3	o.		For alkalization of urine. In 3.8% soln. for prevention of blood clotting, 1/10 of the volume of blood.
Sodium Iodide B.P.	0.025-0.05	0.1-0.2	0.2-0.3	0.2	3	o.	80% iodine. In ½-5% soln.	In water with liquorice extract. For prophylaxis of goitre much smaller quan- tities (ca. 1 mg per week). Cf. Potassium Iodide!
Sodium Salicylate B.P.	0.05-0.1	0.2-0.4	0.5-0.75	0.5	3	o. r.	in 10% soln.	In water with syrup of bitter orange or liquorice extract; if necessary rectal in mucilage using 10% soln. As anti- rheumatic larger doses (0.3 × years o age p.d. in 4-5 doses or more).
Sodium Sulphate B.P.	—	1 teaspoon- ful	1-2teaspoon- fuls		1	o.		In water.
Glauber's Salt								

Stibophen B.P. Fouadin Pentasodium antimonybiscatechol- 3:5-disulphonate	0.1 ml of 6.4% soln. per kg body weight	3.0 ml	daily	i.v.	6.4% soln., 1 ml = 8.5 mg anti- mony (trivalent)	Start with a small dose daily, increasing up to 3rd day, then this last dose every other day. In bilharziasis and leish- maniasis.
Streptomycin B.P. (hydrochloride or sulphate)	In general 20-50 mg/kg body weight p. d. in 2-4 portions up to 0.3 p.d. up to 0.5 p.d. up to 0.8 p.d.	600- 700 mg		i.m.		Synergistic with penicillin, P.A.S., isoni- azid, therefore often in combination.
Strophanthin-K B.P.C. Kombé Strophanthin	0.00003- 0.00005-0.0001 0.000125- 0.0002 (0.000125)- 0.0002-0.0003	0.000125 -0.00025	1	i.v.	Standardized glycoside mixture with activity 40% that of anhyd. ouabain	Caution! Give first a test injection of ca. 1/3 the stated dose and proceed to full dose only if tolerated. Administer slowly, diluted with 10% dextrose, strictly only i.v.! Do not give less than 2 days after taking digitalis. For i.m. injection Myo- kombin (BOEHRINGER) with 0.5% stro- phanthin and 0.07% procaine. Ouabain: half the stated doses and for short time only.
Strychnine nitrate	0.0001-0.0003 0.0005-0.001 0.001-0.002	0.001	1-(2-3)	o.	Granules 0.0005	
Sulphonamides	Sulphanilamide, Sulphapyridine, Sulphapyrimidine, Sulphathiazole: according to severity					
	Sulphanilamide, Sulphapyridine, Succinylsulphathiazole: of infection 0.15-0.2 per kg Initial dose: 1/4-1/2 first daily dose	4.0	daily in 4-6 parts	o.		With plenty of liquid after meals. Re- latively higher doses for infants than for older children! Irgafen (Geigy): only half the stated doses, in 3 portions.
	Sulphaguanidine, Succinylsulphathiazole: according to severity of infection 0.2-0.3 per kg first day, followed by 0.15 per kg p.d. in 4-6 portions. Initial dose: 1/4-1/2 first daily dose	5.0				
Sympatol (LEWIS) Phenylephrine tartrate	3-5 gtt. 0.1-0.2 ml 5-10 gtt. 0.2-0.3 ml 10-15 gtt. 0.3-1.0 ml		2-3 1-2(-3)	o. s.c.	10% soln. amp. 1 ml = 0.06	
Tanninum albuminatum	0.1-0.3 0.2-0.5 0.5-1.0	0.5	3	o.		In cocoa with meals.
Terramycin. See Oxytetracycline Hydrochloride						
Tetrachlorethylene Ethylene tetrachloride	— Cure dose: 8 gtt. for each year of age		*	o.	1.0 = 49 standard drops	* In gelatine capsules after a light break- fast; saline purge after 1 hour. Pre- liminary high-carbohydrate, low-fat diet. In Ancylostoma infections.

Weights are in grams unless otherwise stated.

N.B. In using this table it is important that special attention be paid to the data given in the columns headed "Number of single doses per day" and "Remarks", as well as to the introductory remarks on page 401.

Abbreviations:

amp. = ampule(s)
B.P. = British Pharmacopoeia
B.P.C. = British Pharmaceutical Codex
drag. = dragée(s)
ext. = external
gtt. = drops
inh. = inhalant
i.m. = intramuscular
i.v. = intravenous
I.U. = international units
max. = maximum
mg = milligram(s)
min. = minimum
ml = millilitre(s)
o. = oral
p.d. = per day
p.inf. = pro infantum
P.H. = Pharmacopoea Helvetica
P.I. = Pharmacopoea Internationalis
r. = rectal
s.c. = subcutaneous
soln. = solution
supp. = suppository(ies)
tbl. = tablet(s)
U. = unit(s)
U.S.P. = United States Pharmacopeia
μg = microgram = 0.001 mg

	Single dose (unless otherwise stated) for:				Number of single doses per day	Ad-min-istration	Commercial form, composition, content	Remarks
	3-12 months 5-10 kg 0.35-0.40 m ²	3-5 years 15-20 kg 0.6-0.75 m ²	6-12 years 20-40 kg 0.85-1.3 m ²	1 m ² body surface				
Theobromine and Sodium Salicylate B.P.	0.05-0.1	0.1-0.3	0.3-0.5	0.3	3	o.	ca. 48% theo-bromine	With syrup in water. For 2 days, then intermission, then again 2-3 days, and so on.
Theophylline and Sodium Acetate ...	0.02	0.05	0.1	0.1	2-3	o.	ca. 65% theo-phylline	In water, for 2-3 days, then intermission, then only every other day.
Thiamine. See Vitamin B ₁								
Thyroid B.P.	0.03-0.05	0.06-0.09	0.09-0.12	0.125	daily	o.	0.1 dried thyroid = 0.5 fresh thyroid gland. Thyroxine-iodine content: 0.09-0.11%	Start with a smaller dose and increase gradually under continuous supervision up to sub-toxic dose. Use only standardized preparations!
Thyroxine Di-iodotyrosine di-iodohydroxy-phenyl ether	0.0001	0.0001-0.0005 -0.001	0.0001-0.0005 -0.001	0.0005	daily	o.	65% iodine	Caution, danger of overdoses. Thyroid is preferable. Continuous medical supervision. Increase slowly!
Tinctura Strychni. See Nux Vomica Tincture								
Troxidone B.P. Trimethadione Trimethyloxazolidinedione	15-25 mg/kg body weight p.d. in 2 portions, increasing slowly up to double initial dose			0.6	daily	o.	tbl. 0.15 capsules 0.3	Caution, close medical supervision. Danger of injury to sight and hearing!
Tryparsamide B. P. Sodium p-carbamoylmethylamino-phenylarsonate	0.035-0.045 per kg body weight			1.0	*	i.v.	amp. 1.0, 2.0, 3.0 ca. 25% arsenic	* 1 injection weekly for 3-4 weeks, then 1 month intermission, and so on up to a total of 60-80 injections. In trypanosomiasis. Danger of blindness!
Urea B.P. Carbamide	—	up to 15.0	up to 30.0	up to 30.0	daily	o.		With sugar in water, objectionable taste. After 5 days, several days intermission.
Urethane B.P. Ethyl carbamate	0.5-1.0	1.0-2.0	2.0-3.0		1-2	o.		As mild soporific. In water, also rectal, possibly repeated after 1 hour. As cytostatic different dosage.

Valerian Tincture	5 gtt.	10 gtt.	15-20 gtt.	2-4	o.	1.0 = 53 standard drops = 0.6 fresh valerian	With sugar in water. Also as suppository for infants and young children.
Veriazol (KNOLL)	1-4 gtt.	3-5 gtt.	5-10 gtt.	3	o.	1 ml soln. = 1 tbl. = 1 ml of amp. =	
	0.25 ml	0.25-0.5 ml	0.25-0.5 ml	1	s.c. i.m.	0.1 leptazol plus 0.01 pholedrine sulphate	s.c. or i.m. only in case of collapse!
Vitamins	The daily requirements are given, unless otherwise stated; as therapeutic doses, multiples of the daily requirement must be administered. Care must be taken not to give overdoses of vitamins A and D (for prophylaxis liver oil is therefore preferable)! Administration is usually oral only.						
Vitamin A (axerophthol)	1500-2000 I.U.	2000-2500 I.U.	3500-4500 I.U.	daily		1000 I.U. = 0.6 mg β -carotene = ca. 0.3 mg	Symptoms of overdose: Over-excitability, symmetrical cortical hyperostoses, loss of appetite, loss of hair.
Vitamin B ₁ (aneurine)	0.4-0.6 mg	0.6-0.8 mg	1.5-1.8 mg	daily			
Vitamin B ₂ (riboflavine)	4-6 mg	6-8 mg	10-12 mg	daily			
Vitamin C (ascorbic acid)	30 mg	50 mg	60-75 mg	daily			
Vitamins D ₂ and D ₃	For prophylaxis of rickets: 2400-4000 I.U.	4000-6000 I.U.		daily		1000 I.U. = 0.025 mg	After 3-4 weeks 2 weeks intermission. Large-dose therapy (cave overdose): 600,000 I.U. orally; also i.m. (only D ₃ is effective).
	For therapy of rickets: 8000-16,000 I.U.	8000-16,000 I.U.		daily			Symptoms of overdose: Anorexia, obstipation, vomiting, retardation of growth, osteoporosis, hypercalcaemia (SULKOWITZ reaction in urine positive), calcareous metastases, nephrosis, increase of non-protein nitrogen; renal insufficiency can eventually be fatal.
Vitamin K (analogues: Menaphthone, Synkavit [ROCHE])	Newborn (0.005-0.01)			daily	o. i.m.	tbl. 0.01 amp. 0.01	

Poison

Abortifacients. See under Volatile oils

Acetylcholine, Physostigmine, Pilocarpine.....

Acids

Aconite, Aconitine

Alcohols

Allyl, Amyl

Ethyl (Ethanol)

Methyl (Wood spirit, Methanol)

Alkalis, Caustic soda, Caustic potash

Ammonia, Sal ammoniac (Ammonium chloride)

Aniline, Amidopyrine, Antipyrine (Phenazone), Phenacetin

Apiol. See under Volatile oils

Arsenic, Arsenious acid, FOWLER's solution (Potassium meta-arsenite), Calcium and Lead arsenates (insecticides), Schweinfurt green

Symptoms

Cholinergics; death due to central respiratory paralysis. Pilocarpine as a diaphoretic in cardiac and vascular disease is dangerous (pulmonary oedema). Symptoms: narrowing of the pupils, slowing of the pulse, increase of glandular secretion, nausea, vomiting, diarrhoea, desire to urinate, collapse.—Physostigmine causes fibrillary and fascicular muscle twitchings often persisting long after the poisoning and not completely relieved by atropine.

With nitric acid yellowish sloughs, with sulphuric acid whitish or in severe cases black sloughs, with oxalic acid only slight corrosion. Abdominal pains, vomiting of bloody or brownish masses; cardiac weakness, shock.

Pricking and burning sensation in the mouth, paralysis of tongue and mouth muscles (local effect); after resorption tingling and creeping sensations on the skin, paralysis of facial muscles, intolerable feeling of cold, lowered temperature, green vision, nausea, characteristic cardiac disturbances (first bradycardia, then complete arrhythmia with extrasystoles), loss of consciousness.

As for ethyl alcohol, but markedly more toxic; severe irritation of the mucosa.

Smell of alcohol. Narcosis, areflexia, dilated, staring pupils, difficult respiration, lowered temperature down to 30°C (86° F).

Intoxication usually not so marked as with ethyl alcohol but combined with severe colic pains, nausea, vomiting, central respiratory paralysis. Lethal dose 30–100 ml, less for undernourished persons. Secondary toxic symptoms after a latent period lasting from hours to days: sudden collapse due to dyspnoea, suffocation spasms, visual disturbances (dilated, staring pupils without paralysis of the ocular muscles), often permanent blindness due to optic atrophy. Diagnostically important: formic acid in urine.

The corrosive action of alkalis goes deeper than that of acids. Swollen lips; whitish, yellowish slippery sloughs in the mouth and pharynx, vomiting of greasy masses coloured reddish brown by alkali-haematin, swallowing difficult or impossible, severe pains, often spasms due to alkalosis, death in several hours or days due to shock and collapse, aspiration pneumonia.

Acute: (external) inflammatory erythema, blisters, eyes particularly endangered: turbidity of the cornea, destruction of the whole eyeball. (Internal) lethal dose 5–10 g, glottic oedema or spasms, pulmonary oedema, bloody vomiting, collapse.

Chronic: inflammation of the eyes, turbidity of the cornea, bronchial catarrh, bloody expectoration, digestive troubles, polyps.

Blood poisons; cyanosis, often agranulocytosis, headache, irritation of the bladder, polyuria with watery urine, respiratory difficulties, spasms, collapse, stupor up to complete unconsciousness. (In aniline poisoning the start of drowsiness is often marked by euphoria.) In antipyrine, etc. poisoning the patient usually remains conscious.

Acute: severe headache, nausea, diarrhoea (can be absent), death in several hours due to severe collapse.

Subacute: gastro-intestinal form: severe gastric and intestinal pains, often uncontrollable vomiting and rice-water stools reminiscent of cholera, anuria, calf pains; in slow poisoning inflammation of the mucosa of eyes, nose, pharynx, painful swallowing, tenesmus, lowered temperature, spasms, unconsciousness, lowered blood pressure.

Chronic: irritation of the mucosa and less severe gastro-intestinal disturbances, polyneuritis combined with muscular weakness and atrophy, symmetrical paralysis, mostly starting with the feet, melanosis, symmetrical hyperkeratosis on palms of the hands and soles of the feet, anaemia, icterus. The breath of sufferers from chronic arsenic poisoning often has a smell resembling garlic.

Treatment

Atropine, 1 mg subcutaneous, possibly repeated. Lobeline, nikethamide, oxygen.

Gastric lavage contra-indicated. Neutralization with magnesia, aluminium hydroxide (gel), or possibly soap solution. *No chalk, no sodium bicarbonate, no soda, no lime* (tympaanites). After neutralization demulcents (raw albumin, milk, vegetable oils, etc.), morphine as analgesic, sodium bicarbonate or lactate to relieve acidosis (after oral or i. v. neutralization). *In oxalic acid poisoning* lime water or syrup of lime, calcium i. v., otherwise as above.

Gastric lavage with 1:1000 potassium permanganate, leaving ca. 100 ml in the stomach. Keep patient warm, caffeine subcutaneously or black coffee rectal, other analeptics, oxygen, possibly cardiac therapy. *Emetics contra-indicated.*

As for ethyl alcohol.

Gastric lavage with water, caffeine subcutaneous or black coffee rectal, inspiration of ammonia, analeptics (nikethamide, Sympatol), possibly strophanthin, in cyanosis oxygen, *laevulose* i. v., warmth.

Gastric lavage with 5% sodium bicarbonate solution, leaving 70–100 ml in the stomach. 1000 ml 1/6 molar sodium lactate i. v. or 4 × 4 g sodium bicarbonate orally at 1/4-hour intervals. *Control of alkali reserve.* Continue with calcium or bicarbonate therapy until CO₂ combining capacity of 40–50 vol% is reached. *Laevulose is contra-indicated*, in contrast to ethyl alcohol poisoning.

Contra-indicated: gastric lavage. Neutralization by dilute acetic acid, 0.5% hydrochloric acid, lemon juice, additionally local anaesthetics; after neutralization demulcents (raw albumin, milk, vegetable oils), warmth, shock therapy, morphine in case of very severe pain, depot penicillin as precautionary measure.

Neutralization as for alkalis. Inspiration of steam, in closure of the glottis hypertonic (33–40%) dextrose or calcium gluconate i. v., possibly tracheotomy (rarely necessary), boric acid solution on the eyes; in sal ammoniac poisoning treatment for acidosis.

Gastric lavage with 1:1000 potassium permanganate, leaving ca. 100 ml in the stomach. Warmth, caffeine or black coffee (the latter possibly rectal), oxygen, possibly artificial respiration, *depot penicillin as precautionary measure.*

Gastric lavage with large quantities of warm water. Subsequently milk of magnesia (20:500) with teaspoonfuls of charcoal, followed by raw albumin, milk, vegetable oils, morphine in case of pain. Shock therapy. When gastric lavage is impossible, emetics.

As soon as possible: BAL therapy: 10% solution in oil with 20% benzyl benzoate; dose (mg pure BAL): 3 mg/kg i. m. every 4 hours for the first 2 days, on third day 4 such injections, then 2 such injections per day for 10 days.

¹) Reviews: FÜHNER, W., *Medizinische Toxikologie*, Stuttgart, 1951; VON OETTINGEN, W. F., *Poisoning*, New York, 1952; CONN, F., *Current Therapy*, Philadelphia, 1955.

Poison	Symptoms	Treatment
Arsine, Arsenic hydride	Some hours after inhalation drowsiness, headache, sensation of cold and anxiety, nausea, vomiting, pain in the upper abdomen, followed shortly by icterus and as most important symptom dark brown urine (haemolysis), anaemia, anuria, uraemia, after recovery often permanent heart and liver injury.	Oxygen, injection of hypertonic dextrose solution with addition of insulin, alkalization. <i>Without delay: BAL therapy as in arsenic poisoning.</i>
Atropine, Belladonna, Hyoscine	Nausea, vomiting, failure of tear and saliva secretion, accommodation disturbances, vertigo, spasms, hallucinations, garrulity, laughing attacks, senseless movements up to frenzy, in children often tremors and continuous movements of the arms and legs (carphology).	Gastric lavage often impracticable: apomorphine hydrochloride (adults 6 mg subcutaneous). <i>Pilocarpine</i> (adults 10 mg subcutaneous), repeat injections until salivary secretion returns. Warmth, oxygen/carbon dioxide, if impossible lobeline, artificial respiration.
Barbiturates, Ureides¹	Acute: unconsciousness and narcosis with absence of reflexes, pupils as in morphine poisoning narrow and without reaction, occasionally hippus, lowered temperature, followed in the first few days by fever, death in coma following circulatory failure and central respiratory paralysis. Chronic: indifference, more or less pronounced intoxication, shuffling gait, impairment of speech, trembling, diplopia, euphoria up to delirium and hallucinations.	1. In tracheal obstruction ensure adequate access of air by endotracheal intubation. Frequent aspiration of secretions. Continuous oxygen administration (in pulmonary oedema avoid positive oxygen pressure). 2. Shock treatment with plasma or whole blood. 3. Central analeptics. Picrotoxin or amphetamine. Picrotoxin: 1 mg each minute i. v. until the pain reflex returns. After recovery of consciousness 6 mg every 30 minutes. If picrotoxin causes convulsions (very dangerous! Caution with dosage) then phenobarbitone. Amphetamine: initially 40 mg i. v., then 30 mg i. v. every 30 minutes. The more severe the barbiturate poisoning the larger are the amphetamine doses which can be tolerated. It is soon seen whether higher doses can be tolerated (up to 100 mg every 30–60 minutes). Continuous medical attention necessary with picrotoxin and amphetamine treatment! 4. Gastric lavage during the first two hours with potassium permanganate 1:1000, leaving ca. 100 ml in the stomach. Barbiturates cause irritation of the stomach and pylorospasm. 5. Adequate liquid administration i. v. 6. Urethral catheterization, mercury diuretics. The KOLFF-type artificial kidney is very effective and eliminates more barbiturates in one hour than the natural kidney in 24 hours (see bibliography: KYLE et al.; ALLWALL and LUNDERQUIST). 7. Saline purges. 8. Depot penicillin as precautionary measure. For bibliography see footnote.
Barium oxide, hydroxide, chloride, carbonate	Barium hydroxide is caustic and has a corrosive action on the mucosa. Oral poisoning: gastric pains, nausea, vomiting, diarrhoea similar to that in arsenic poisoning, but with increase of blood pressure. Other symptoms as in digitalis poisoning: bradycardia or tachycardia, palpitations, vertigo, cold sweat, death not preceded by loss of consciousness. In slow poisoning characteristic progressive paralysis: legs, arms, neck muscles, tongue. In rapid poisoning death due to heart failure, in slow poisoning to respiratory failure.	Evacuation of the stomach, sodium sulphate in purgative doses (10–30 g in plenty of water) and in 2% solution i. v. (isotonic). In case of barium hydroxide ½% sulphuric acid orally. Analeptics, possibly oxygen.
Belladonna. See under Atropine		
Botulism	Usually affects small groups of persons simultaneously following eating of home-preserved beans or bean salad, tainted meat preserves (rare), when eaten uncooked (botulin is destroyed by cooking). Tainted foods do not show obvious putrefaction but at the most a rancid smell. Incubation time 12–24 hours. Diffuse paralysis without increase of temperature (bulbar paralysis), accommodation disturbances, lack of pupillary reaction, but in contrast to atropine poisoning combined with ptosis, marked hoarseness and speech impairment, sphincter paralysis, obstipation, anuria. Death after several days with complete consciousness.	<i>Antitoxin</i> , charcoal, castor oil, dextrose, strophanthin.
Bromides, Potassium, Sodium, Calcium and Ammonium bromides	Acute poisoning is rare. More frequent is brominism (in epileptics): similar to iodine poisoning but less common; rhinitis or coughing; frequently bromine acne (inflammation of the hair follicles), various sorts of skin eruptions, loss of appetite, loss of memory, indifference to surroundings, disturbances of vision, speech, perception and movement, acute psychosis with dementia, loss of bodily strength.	For <i>non-epileptics</i> : compel patient to drink 3–4 litres of water per day with much salt (30–40 g). For calming excitation 5–15 ml paraldehyde orally or 30 ml in 60 ml olive oil rectal.
Camphor. See under Volatile oils		
Carbon monoxide, Domestic gas	Headache, nausea, cherry-red skin and mucosa, then cyanosis. Respiratory disturbances, paralysis, spasms, loss of consciousness.	Fresh air, <i>oxygen/carbon dioxide</i> , in serious cases blood-letting and transfusion, analeptics.

¹) Bibliography: ALLWALL and LUNDERQUIST, *Lancet*, **1**, 446, 1953. DICK, H. L. H., *Amer. J. med. Sci.*, **224**, 281, 1952. FREIREICH and LANDSBERG, *J. Amer. med. Ass.*, **131**, 661, 1946. FRIEDMANN and HARRIS, *Amer. J. med. Sci.*, **221**, 133, 1951. KYLE et al., *J. clin. Invest.*, **32**, 364, 1953. MAYER and BEITMAN, *Harper Hosp. Bull.*, **7**, 311, 1949. REED et al., *Ann. intern. Med.*, **37**, 290, 1952. RISCHKE, J., *Ugeskr. Laeg.*, **112**, 507, 1950.

Poison	Symptoms	Treatment
Carbon tetrachloride, Chloroform	Drowsiness, headache, nausea, vomiting, twitchings and spasms, tendency to bleeding, enlargement of the liver, icterus, cardiac weakness, anuria.	Gastric lavage with vegetable oils or medicinal paraffin (<i>carefully remove all oil</i>), charcoal, <i>atropine 1 mg subcutaneous</i> , central analeptics, calcium therapy i. v., vitamin K, vitamin B ₁₂ , choline.
Caustic potash, Caustic soda. See under Alkalis		
Chenopodium oil. See under Volatile oils		
Chloral hydrate	Overdosage can cause heart failure, liver damage.	Central analeptics, cardiac stimulants.
Chlorine	Irritation of the mucosa, coughing, rhinitis, lacrimation, in prolonged exposure pronounced secretion in the respiratory passages, becoming bloody with high concentrations. Pneumonia, pulmonary oedema rare.	Complete rest, <i>avoid artificial respiration or administration of oxygen under pressure</i> . Breathing of alcohol vapour, oxygen, inhalation of 1% sodium thiosulphate, depot penicillin as precautionary measure.
Chloroform. See under Carbon tetrachloride		
Chromic acid, Potassium dichromate	Abdominal pains, nausea, vomiting of yellow to greenish masses. Collapse or diarrhoea with slimy and bloody faeces, haematuria, death from anuria and uraemia.	Gastric lavage, demulcents (raw albumin, milk), milk of magnesia (20:500) in teaspoonfuls, morphine for relief of pain.
Cocaine, Procaine	Dryness of the throat, nausea, buzzing in the ears, intoxication, respiratory disturbances, tachycardia, convulsions, collapse.	Gastric lavage with copious warm water, then tannin solution. Artificial respiration, oxygen, for convulsions chloral hydrate, phenobarbitone, possibly analeptics.
Corrosive sublimate. See under Mercury		
Cyanides. See under Prussic acid		
Digitalis, Foxglove	Nausea, vomiting, diarrhoea; slowing of pulse to 40–50, at this stage extrasystoles, subsequently quickening with soft, thready, very fast (up to 140) pulse, fall in blood pressure, death in from one to several days. Secondary symptoms: cyanosis, anxiety, extreme weakness, coloured vision, cold sweat, vertigo, delirium, hallucinations, anuria.	Gastric lavage with charcoal or sodium sulphate. <i>Very complete rest</i> . Relief of vomiting with atropine-hyoscine, of anxiety with amyl nitrite, oxygen, caffeine.
Essential oils, Ethereal oils. See under Volatile oils		
Ethyl alcohol. See under Alcohols		
Ethylene glycol, Diethylene glycol, Dioxan	Slow intoxication, unconsciousness, liver injury, anuria.	Evacuation of the stomach, central analeptics, oxygen, prevention of acidosis.
Fluorides, Sodium fluoride . . .	Pruritus, nausea, vomiting of slimy, then bloody masses, strong salivation, severe abdominal pains, bloody diarrhoea with unquenchable thirst, pupillary paralysis, ptosis, convulsions, death from heart or respiratory failure.	Gastric lavage with milk, or if unavailable, repeatedly with little water which must be removed immediately. Morphine for relief of pain, <i>large doses of calcium i. v.</i> , shock therapy, stimulants. For 48 hours copious milk and raw albumin. Continue calcium therapy until fully recovered.
Food poisoning. See Botulism		
Formaldehyde, Formalin	Choking spasms, rapid suffocation; in less severe cases bloody vomiting, intoxication, drowsiness, albuminuria, anuria, pulmonary and cerebral oedema.	Gastric lavage with 0.2% ammonia, subsequently copious raw albumin, milk or other proteins in solution, collapse therapy. Subsequently 20–30 g urca in aqueous solution orally, if pulmonary oedema indicated hypertonic dextrose solution i. v.
FOWLER's solution. See under Arsenic		
Gas, domestic. See under Carbon monoxide		
Gasoline. See Petroleum spirit		
Hyoscine. See under Atropine		
Iodine	Burning sensation in the throat, rhinitis, coughing, conjunctivitis, vomiting, abdominal pains, diarrhoea, psychic disturbances, collapse.	Gastric lavage with starch suspension, preferably first boiled, until it no longer turns blue. Subsequently raw albumin, milk, analeptics, calcium therapy i. v.
Lead, White lead (Lead Carbonate), Lead chromate (Chrome yellow), Lead antimonate, Lead arsenate (see under Arsenic), Lead acetate, Lead water (1:50 dilution of 40% lead acetate), Tetraethyl-lead (anti-knock agent in petrol)	Acute: slower course than mercury poisoning, death only after 2–3 days. Nausea, increased salivation, unpleasant sweetish mouth odour, vomiting, severe abdominal pains, spastic obstipation, anuria. Very marked bodily weakness, lowered blood pressure, soft pulse, lowered temperature. – In poisoning by tetraethyl-lead nervous symptoms predominate, without intestinal spasms: loss of appetite, nausea, lowered temperature and blood pressure, severe insomnia, continuous excitement, hallucinations, delirium resembling alcoholic delirium. Chronic: marked pallor in early stages, yellowish-livid skin coloration, metallic taste, lead line, basophilic stippling of the erythrocytes, porphyrinuria, extensor weakness, finally as late symptom paralysis of the wrist. Lead colic, enlargement of the liver, also icterus instead of skin coloration; lead nephritis, kidney sclerosis, lead gout. – Visual disturbances, hand tremors, encephalopathy, epileptiform convulsions, delirious attacks, anxiety, usually sexual impotence.	Acute: gastric lavage with 2–3% sodium sulphate solution and charcoal. As purgative magnesium sulphate. Subsequently raw albumin, milk, etc., calcium in large doses i. v. Acute and chronic: immobilization of the lead in the bones by a high-calcium diet, calcium i. v. and moderate doses of vitamin D. Recovery in 3–6 weeks, then deleading treatment: diet low in vitamin D and calcium, protection from light, ca. 45 drops per day saturated potassium iodide solution, parathyroid hormone (duration of cure ca. 3–4 days). If necessary repeat both cures. Vitamin B ₁ and whole B-complex.
Luminal. See under Barbiturates		

Poison	Symptoms	Treatment
Mercury, Corrosive sublimate (Mercuric chloride)	Acute and subacute: burning sensation in oesophagus and stomach, nausea; vomiting of masses at first slimy, later bloody; abdominal pains, black diarrhoea (in the case of calomel, green); initially increased, then decreased diuresis, anuria. In prolonged poisoning stomatitis, redness of pharyngeal mucosa, exanthema. Chronic: Most obvious are symptoms of damage to central nervous system: headache, polyneuritis. Metallic taste, loosening of the teeth, persistent catarrh, erethism, fine tremors (shaky handwriting), psychic weakness, increasing cachexia, intolerance of alcohol and tobacco, sensitivity to infections, particularly tuberculosis.	In acute poisoning gastric lavage with saturated sodium bicarbonate solution, at least 4 litres, leaving 200 ml in the stomach. Shock therapy, relief of pain with morphine. <i>Without delay BAL</i> : 5 mg/kg in one dose i.m. (see under Arsenic), subsequently as in arsenic poisoning. Precautions against acidosis, keep urine alkaline.
Meta (Metaldehyde)	Nausea, vomiting, exaggerated reflexes up to epileptic and tetanic convulsions, trismus, biting of the tongue, opisthotonus.	Cautious gastric lavage with addition of charcoal, saline purges; for convulsions phenobarbitone or rectal chloral; 2% sodium phosphate solution and 5% dextrose solution i.v. Heart stimulants, analeptics.
Morphine, Opium, Codeine, Heroin, etc., Dilaudid, Dromoran, Demerol, Methadone, etc. ¹	Profuse sweating, severe pruritus, sometimes slowing of pulse, intoxication, miosis, profound unconsciousness, lowered temperature, absence of reflexes, coma, respiratory paralysis. Diagnostically important: pupils; retention of urine and faeces.	<i>Antidote for morphine, opiates and similar substances</i> (but not barbiturates): <i>N</i> -allylnormorphine 2.5 to 10 mg several times s.c. according to degree of poisoning ¹ .—Gastric lavage (also for subcutaneously injected poison) with 4–5 litres 1:1000 potassium permanganate solution, followed by instillation of a mixture of 50 ml 20% charcoal suspension and 50 ml 50% magnesium sulphate solution. Oxygen, depot penicillin as precautionary measure.
Mushrooms (Toadstools) Edible turban-top (helvellic acid)	4–8 hours after eating, abdominal pains, nausea, vomiting, diarrhoea with rice-water stools. These symptoms last for 1–2 days, followed by increasing injury to liver and kidneys. Icterus, possibly resulting in yellow atrophy of the liver. Helvellic acid occurs in small quantities in other fungi, e.g. goat's beard, particularly in older specimens, but its toxicity is only apparent when large quantities are consumed since it is largely destroyed by cooking and drying.	Use of emetics, purgatives, adsorption is usually too late. Precautions against dehydration. Rarely has fatal outcome.
Amanita <i>Amanita phalloides</i> (white or deadly amanita, death cup) is often mistaken for the edible mushroom, the yellowish and greenish varieties for <i>Tricholoma</i>	After a latent period of 8–10 hours usually without prodromal signs, sudden nausea, abdominal pains, usually diarrhoea. Uncontrollable vomiting and rice-water stools reminiscent of cholera or arsenic poisoning. Water impoverishment, enlargement of the liver, calf cramps, increasing drowsiness, delusions, death in about 5 days, later unlikely. The most dangerous of European poisonous fungi, responsible for nearly all deaths from this cause.—Anatomicopathologically amanita poisoning cannot be distinguished from phosphorus poisoning. Evidence is provided by presence of spores in the intestine or vomit.	Emetics, gastric lavage, etc. are useless. Sugar therapy with dextrose infusions for several days, insulin, copious infusions of physiological salt solution, cortisone, vitamin B ₁₂ , analeptics, calcium therapy, chloral hydrate for relief of vomiting.
<i>Amanita muscaria</i> (fly agaric), <i>Amanita pantherina</i> , etc. (muscarine, muscaridine)	Often harmless; often symptoms resembling atropine or pilocarpine poisoning, frequently combined: excessive salivation, fever, severe sweating, narrowing of the pupils, cyanosis, pulmonary oedema, clonic spasms, intoxication, delirium, collapse, no liver injury.	Symptoms appear early, hence gastric lavage, charcoal, etc. often successful. Analeptics, phenobarbitone or atropine or both, according to the clinical picture. Rarely fatal.
Boletus	Symptoms as with amanita but appearing after about one hour. Removal of poison therefore possible.	
Naphthalene (Moth balls)	Headache, nausea, vomiting, renal injury (albuminuria, haematuria), turbidity of the lens, optic neuritis.	Gastric lavage with copious warm water, followed by charcoal, plenty of raw albumin, analeptics.
Nicotine, Tobacco	Nausea, vomiting, malaise, anxiety, sensation of cold, cardiac weakness, collapse, obstipation or diarrhoea.	Gastric lavage with 2% tannin solution, alcohol, caffeine subcutaneously, opiates for relief of abdominal pains, oxygen; keep lower abdomen warm.
Nitrous fumes	In high concentrations severe coughing, haemoptysis, pulmonary oedema; in lower concentrations latent period of 6–12 hours, then dyspnoea, cyanosis, bloody expectoration, pulmonary oedema.	<i>Absolute rest, oxygen without positive pressure, warmth, blood-letting, hypertonic dextrose solution i.v., inhalation of sal ammoniac vapour.</i> Codeine for relief of pain and coughing; analeptics; trophanthin.
Nux vomica. See under Strychnine		
Oxalic acid. See under Acids		
Petroleum spirit, Benzene, Toluene, Xylene (see also Tetraethyl-lead under Lead)	Euphoric intoxication, convulsive stage, complete narcosis. Chronic: feebleness, vertigo, head and gastric pains, vomiting, pollution of blood: initially leuko- and thrombopenia, often also lymphocytosis, fall in erythrocytes and haemoglobin, aplastic anaemia. Tendency to bleeding in oral mucosa, nose, stomach, intestine, female genitals; idiopathic purpura, fatty degeneration of vessels, alcohol intolerance.	Poisoning by vapour: <i>oxygen tent</i> , if impossible artificial respiration, lobeline, nikethamide, leptazol. Poisoning by drinking: gastric lavage with 5% sodium bicarbonate solution and 3% charcoal suspension, leaving 200–300 ml of latter in the stomach. Respiration as for vapour. Blood transfusion, <i>depot penicillin as precautionary measure</i> , alkalization, vitamin K.
Phenobarbitone. See under Barbiturates		

¹) Bibliography: UNNA, K., *J. Pharmacol.*, **79**, 27, 1943. HART and McCawley, *ibid.*, **82**, 339, 1944. HUGGINS et al., *Proc. Soc. exp. Biol.*, **75**, 540, 1950. SMITH et al., *Fed. Proc.*, **10**, 335, 1951. CHASE and BOYD, *J. Amer. med. Ass.*, **150**, 1103, 1952. ECKENHOFF et al., *Amer. J. med. Sci.*, **223**, 191, 1952. FRASER et al., *J. Amer. med. Ass.*, **148**, 1205, 1952. MARX and LOVE, *Ann. intern. Med.*, **39**, 635, 1953.

Poison	Symptoms	Treatment
Phosgene	Symptoms appear only after a latent period of several hours. Death from pulmonary oedema, brownish foaming from mouth and nose, increasing cyanosis, quickening of pulse. If not fatal in a few days, good prospects of recovery.	<i>Absolute rest, warmth, oxygen without positive pressure</i> , injection of hypertonic dextrose solution, followed by calcium i. v., vitamin C in large doses, extensive blood-letting. Avoid artificial respiration and morphine. Codeine or hexobarbitone for relief of coughing, cardiac stimulants.
Potassium dichromate. See under Chromic acid		
Procaine. See under Cocaine		
Prussic acid, Potassium cyanide, Bitter almonds and oil, Linseed	Acute poisoning with prussic acid or cyanides is rapidly fatal and treatment is usually too late to be of help. In less serious cases: unconsciousness, convulsions, bright red blood, respiratory paralysis.	Artificial respiration, oxygen/carbon dioxide, lobeline. Increase of the blood pressure, if necessary by intracardial adrenaline. When breathing recommences gastric lavage (not in case of prussic acid) with 1:1000 potassium permanganate. 5% sodium thiosulphate i. v. up to a total of 20 g thiosulphate, inhalation of amyl nitrite or 20 ml 1% sodium nitrite i.v., blood transfusion, 5% dextrose i.v., methylene blue i.v.
Pyramidone. See under Aniline		
Salicylates	Poisoning usually due to accumulation as a result of delayed elimination by the kidneys; drowsiness, headache, deafness, buzzing in the ears, also visual disturbances, copious sweating; fall in blood prothrombin level: tendency to bleeding in the mucosa; delirium, death with collapse. Often urticaria, albuminuria, haematuria.	Gastric lavage with charcoal, milk of magnesia. Saline purges, precautions against acidosis, collapse therapy, precautions against dehydration, vitamin K.
Santonin, Chenopodium oil. See under Volatile oils		
Scopolamine. See under Atropine		
Snake-bite	In Europe mostly by adders and vipers.	1. Antiserum. 2. Tourniquet, incision, sucking-out of venom, possibly injection of potassium permanganate solution. 3. ACTH (corticotropin) or cortisone or hydrocortisone in large doses. 4. Analeptics: respiratory and cardiac stimulants. Sedatives for relief of anxiety.
Strychnine, Nux vomica	Exaggeration of reflexes, anxiety, speech impairment, dyspnoea, stiffness and pulling in the jaw and neck muscles, trismus, tetanic convulsions provoked by external stimuli, opisthotonus, arrest of respiration during convulsions, cyanosis, consciousness fully maintained. The convulsions can reoccur over a long period according to the amount of poison received. Doses of the order of 1 g cause death in 1/2 hour without onset of convulsions.	Initially relief of convulsions by cautious chloroforming or with ether, together with phenobarbitone i.v. or similar sedatives. Narcosis should be ceased as soon as sedatives take effect. Gastric lavage with 5% sodium bicarbonate. Oxygen, <i>absolute rest, darkness</i> . Calcium therapy i.v., sodium bicarbonate i.v., in recurrence of convulsions sedatives again.
Thallium	Acute: nausea, vomiting, abdominal pains, muscle twitchings, depression, dementia, death in coma. In less acute cases: after 24 hours, nervous pain, deafness, formication in fingers and toes, clawhand and clawfoot. Nausea, diarrhoea and vomiting similar to arsenic poisoning. Characteristic obstipation with abdominal pains reminiscent of lead poisoning. Excitation of sympathicus: inhibition of sweat secretion, often dilatation of the pupils, vasoconstriction, tachycardia, polyuria. Kidney injury: albuminuria and granular cylinders.—After the first few days, polyneuritis, extraordinarily painful in the foot and calf region as well as in the joints. Standing or standing up is made almost impossible by pain. Sense of touch is reduced, but the skin is hypersensitive to contact, especially on the soles of the feet, upper thighs and abdomen, and even the pressure of clothes and bed can be intolerable. Motor paralyses follow with disturbance of nerve sensibility and loss of tendon reflexes. Pains are hardly relieved by morphine and insomnia hardly overcome by soporifics. Visual disturbances often appearing as early as the first week, optical degeneration with possible eventual blindness, sometimes ptosis. Hyperkeratosis of palms of the hands and soles of the feet, muscle twitchings, encephalitis. Loss of hair after ca. 3 weeks.	Purging with 20–30 g magnesium sulphate (gastric lavage if it still appears possible to remove poison), Carlsbad salt, milk. Atropine for relief of intestinal colic, potassium iodide and diuretics, sodium thiosulphate in dextrose solution i. v., vitamins B ₁ and B ₁₂ , warmth, treatment as in lead poisoning should be tried (immobilization of thallium in the bones with vitamin D and calcium therapy, removal with parathyroid hormone).
Toadstools. See Mushrooms		
Tobacco. See under Nicotine		
Turpentine. See under Volatile oils		
Veronal. See under Barbiturates		
Volatile oils, Apiol, Eucalyptus, Camphor, Turpentine, Mustard oil	Lethal doses average 10–20 g orally, with turpentine 40–120 g. In less serious cases excitation, nausea, headache, intoxication with delusions and hallucinations; in severe cases gastroenteritis, kidney injury, epileptiform convulsions, anuria, narcosis, respiratory paralysis. Apiol causes muscular paralysis.	Gastric lavage with vegetable oils, <i>taking care that all oil is subsequently removed</i> . Otherwise emetics, apomorphine hydrochloride (adults 6 mg subcutaneously), analeptics, phenobarbitone sodium for convulsions, oxygen.

Supplement

Contents

Constituents of Living Matter	427	The Pentose-Phosphate Cycle	499
Carbohydrates	427	Formation of Glucuronic Acid	501
Monosaccharides	427	Extension of Carbon Chains by Carbon Dioxide Fixation	502
Stereochemistry of Sugars	427	Formation of Lecithin and Cephalin	502
Sugar Phosphates	430	Formation of Neutral Fat	503
Polyhydric Alcohols	431	Formation of Cholesterol	503
Oxidation Products of Carbohydrates	431	Synthesis and Metabolism of Steroids of the Adrenal Cortex	503
Oligosaccharides	431	Synthesis and Metabolism of Estrogens	507
Polysaccharides	431	Formation of Glutamic Acid	507
Amino Acids	445	Formation of Serine and Glycine	507
Amino Acids Occurring as Protein Constituents	446	Formation of Proline and Hydroxyproline	507
Free Amino Acids	450	Synthesis of Cell Constituents from Amino Acids	508
Nucleotides and Related Substances	452	Formation of Purines	509
Nucleosides and Nucleotides	452	Formation of Porphyrins	511
Nucleic Acids	452	Formation of Creatine	511
Enzymes	467	Formation of Glutathione	512
Nomenclature and Action	467	Formation of Bile Acid Conjugates	512
Enzyme Kinetics	467	Formation of Taurine	512
Metabolism	470	Formation of Pyrimidines	513
General Aspects	470	Formation of Adrenaline and Noradrenaline	513
Energy-Supplying Reactions	472	Formation of Thyroid Hormones	514
Intermediary Stages of Carbohydrate Degradation	472	Formation of Melanin	514
Oxidative Degradation of Fat	474	Formation and Degradation of 5-Hydroxytryptamine ..	514
Degradation of Amino Acids	476	Gluconeogenesis	514
Degradation of Food Constituents	482	Detoxication Mechanisms	516
Mechanism of Biological Oxidations	485	Synthesis of Urea	516
The Key Position of Adenosine Triphosphate	486	Acetylation of Amines	518
Digestive Enzymes	487	Formation of Glycine Conjugates	519
Synthesis of Cell Constituents	499	Formation of Sulfuric Acid Esters	519
Synthesis of Cell Constituents from Glucose	499	Formation of Phenacetylglutamine	519
		Formation of Mercapturic Acids	519
		Index	520

This section, Constituents of Living Matter, has been written in consultation with Professor Sir H. A. KREBS, F. R. S., Dr. K. BURTON, Dr. H. L. KORNBERG, Dr. J. M. LOWENSTEIN* and Dr. J. R. QUAYLE, Department of Biochemistry, University of Oxford, England.

A separate index to this section and to that on Metabolism (pages 470-519) will be found on pages 520-528.

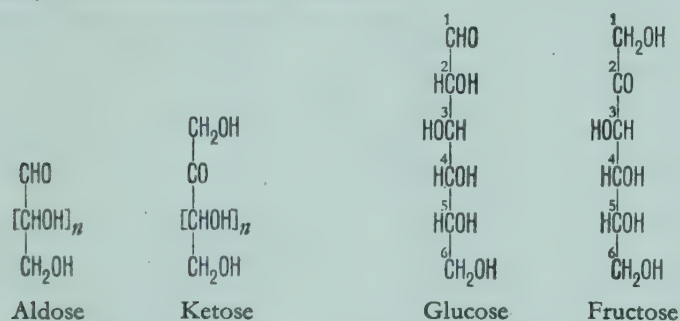
1. Carbohydrates¹

Carbohydrates are carbon compounds which contain hydrogen and oxygen in the ratio 2:1, their general empirical formula being $C_x(H_2O)_y$ ^{**}. The term is also extended, however, to oxidation and reduction products of carbohydrates proper, as well as to their simple derivatives such as amino and phosphorylated sugars.

Carbohydrates are frequently referred to as "sugars" (saccharides) because many of them possess a sweet taste^{***} but actually the term "sugar" is only loosely defined and may denote a wide variety of carbohydrate compounds. To the carbohydrate chemist, however, it means a mono- or oligo-saccharide but *not* a polysaccharide (see below). Mono- and oligosaccharides are given names with the suffix "-ose", e.g. glucose, fructose, lactose.

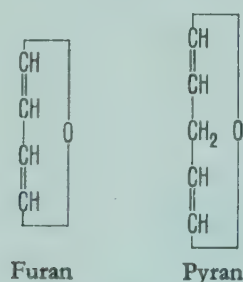
Monosaccharides

Carbohydrates which cannot be split further by hydrolysis are called simple sugars or monosaccharides. Their general empirical formula is $[C(H_2O)]_n$ and they are classed as aldehydic alcohols (aldoses) or ketonic alcohols (ketoses).



Sugars with chain lengths of 3, 4, 5, 6, etc. carbon atoms are known as trioses, tetroses, pentoses, hexoses, etc.[†] The numbering convention is shown above in the structures of glucose and fructose.

The open-chain form of sugars (aldehyde or ketone form) normally occurs only in aqueous solution, where it is a transitional form in equilibrium with the ring form. The latter is the rule with carbohydrates of longer chain length, and with few exceptions the ring is usually 5- or 6-membered. By analogy with the similar heterocyclic compounds^{††} furan and pyran, these ring forms are known as *furanoses* and *pyranoses* respectively:



The ring forms are formed from chain forms by the reaction of the hydroxyl group in the 4 or 5 position with the carbonyl group. Carbon atom 4 is involved in the case of furanoses, carbon atom 5 in the case of pyranoses. This results in the formation of an oxygen bridge between the carbon atoms concerned and of a hydroxyl group on the carbon atom of the original carbonyl group:

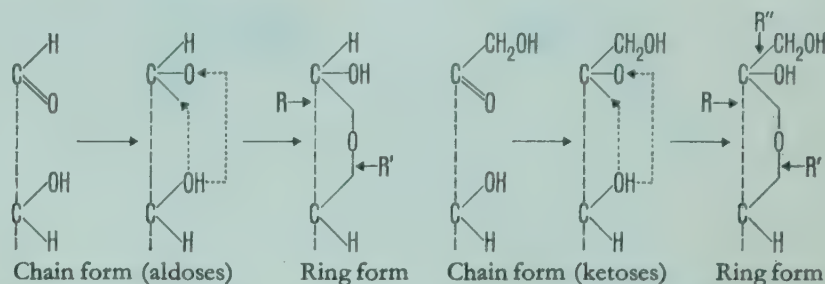
* Present address: Graduate Department of Biochemistry, Brandeis University, Waltham, Mass., U. S. A.

** There are, however, compounds with this empirical formula which do not fall into the category of carbohydrates such as, for example, acetic acid, lactic acid, phloroglucinol.

*** The sweetest of the sugars is fructose. Polysaccharides have no taste.

† According to BEILSTEIN (1938) these names are derived from the number of oxygen atoms. In the case of "ordinary" monosaccharides $[C(H_2O)]_n$, both nomenclatures are identical. They are different in the case of substituted and desoxy sugars. In general the nomenclature which is based on the number of carbon atoms is the more commonly used and permits a better understanding of carbohydrate metabolism (anabolism of the carbon chain from small molecules and its subsequent catabolism).

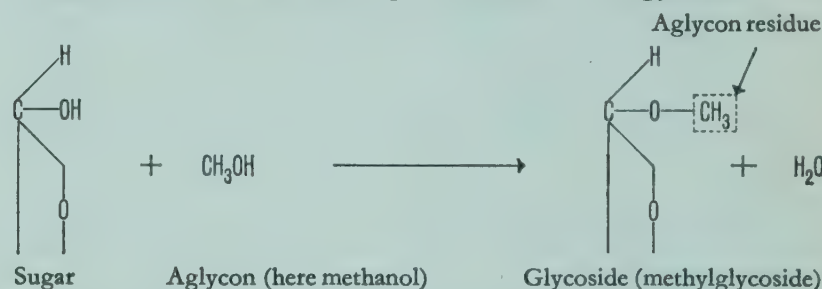
†† Heterocycles are ring molecules in which apart from carbon atoms the ring contains at least one atom of another element.



The compound formed is an intramolecular hemiacetal (when derived from an aldose) or hemiketal (when derived from a ketose).



The hydroxyl group attached to the hemiacetal or hemiketal carbon atom (C-1 or C-2 respectively) is particularly reactive and is known as the glycosidic hydroxyl. It combines readily with the alcoholic or phenolic groups of other molecules, and when this reaction takes place with a compound which is not another sugar (an aglycon), the resulting compound is known as a *glycoside*:



When the reaction takes place with a molecule of another sugar the resulting compound is known not as a glycoside but as a disaccharide (cf. Oligo- and Poly-saccharides, below).

Stereochemistry of sugars

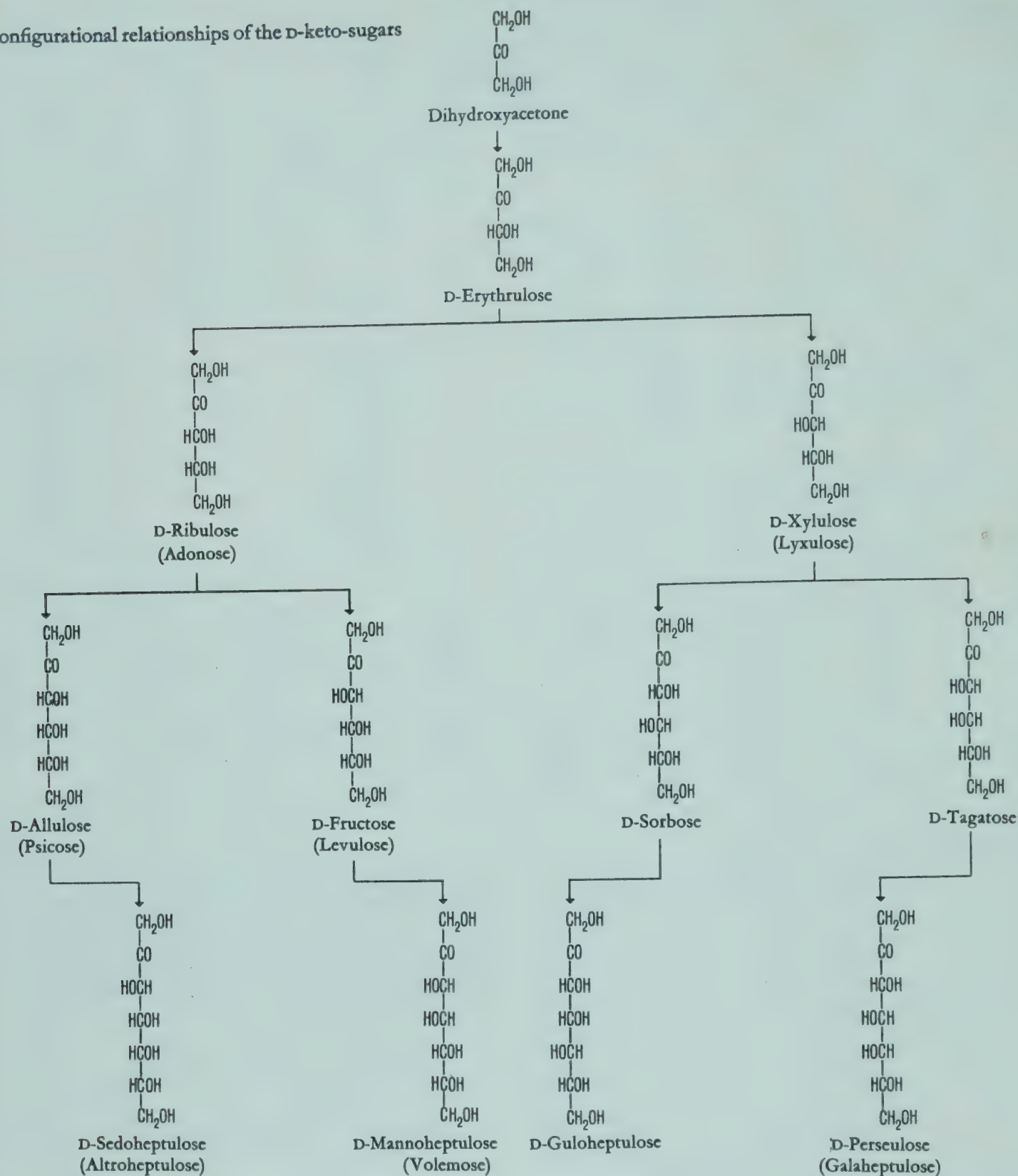
The stereoisomerism of sugars and related substances is of particular importance in biochemistry*, and for this reason it will be dealt with in some detail here. For a more thorough treatment of the subject see HONEYMAN². A carbon atom with four different substituents, for example C-2 of glyceraldehyde, is known as an *asymmetric* carbon atom. This grouping cannot be superimposed on its mirror image and the resulting lack of symmetry gives rise to a type of isomerism which is associated with optical activity. The two possible spatial configurations of the substituents can be readily seen if one imagines the asymmetric C atom to be in the middle of a regular tetrahedron with the valencies pointing to the corners. The two possible configurations of glyceraldehyde which are shown as an example in Figure 1 cannot in any way be superimposed one upon the other. They are related to one another as an object to its mirror image, and are known as enantiomorphs. No such asymmetry exists with a carbon atom possessing at least two identical substituents.

Enantiomorphous isomers are optically active, i.e. in solution one of the isomers rotates the plane of polarized light to the right, the other an equal amount to the left. The degree of rotation depends on the length of the polarimeter tube, on the wave length of the polarized light, on the concentration, and on the solvent and its temperature^{**}. The direction of rotation was originally indicated by

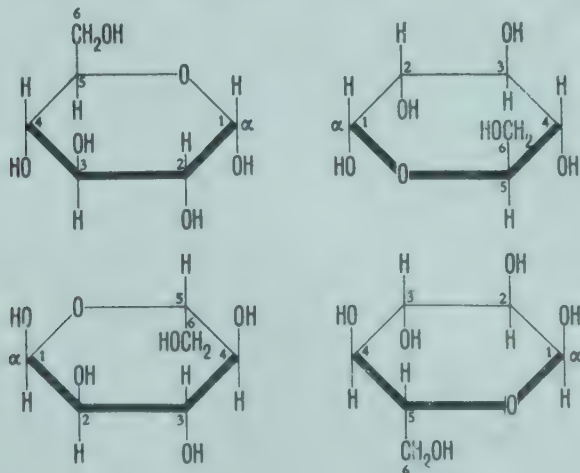
* Stereoisomerism is of importance in nature not only in the case of carbohydrates but for all compounds where stereoisomers are possible. This is because as a rule only specific stereoisomers are synthesized or degraded in naturally occurring reactions (this is a characteristic difference compared to laboratory synthesis). One reason is the stereospecificity of many enzymes, but the fundamental mechanism is unknown.

** The specific rotation $[\alpha]$ is defined as the rotation in degrees of 1 g of substance in 1 ml of solution in a tube with a length of 10 cm. The D-line of sodium is as a rule used as a source of light. The temperature wave length of the incident light, nature of solvent and the concentration must also be included where these diverge from the definition, e.g. $[\alpha]_D^{25}$, 20% (H₂O) = + 12°.

Fig. 3 Configurational relationships of the D-keto-sugars



For convenience in writing the formulas of polysaccharides and other complex sugar compounds, the HAWORTH rings are sometimes written upside down or back to front with respect to the examples shown above, i.e. in the positions obtained by rotating the ring through 180° about two axes in the plane of the ring or about an axis passing vertically through the center of it. The alternative positions for α -D-glucopyranose are as follows:



It is now known that the pyranose ring is not planar, and most of its properties can be explained on the assumption that it has the "chair" form. The furanose ring is usually planar. For further information see MILLS⁶.

The monosaccharides of importance to mammals are listed in Table 1 (pages 432-34). The newer techniques of chromatography have found extensive application in the analysis of sugars⁷, and many specific color reactions have been developed⁸.

Sugar phosphates⁹

Phosphorylated sugars are intermediates in glycolysis; they are components of nucleic acids, nucleotides and polysaccharides¹⁰ (see Table 2, pages 435-38).

The separation of sugar phosphates by paper chromatography¹¹, electrophoresis¹² and ion-exchange chromatography¹³ has been extensively developed in recent years. The quantitative determination of phosphate is usually carried out by spectrophotometric measurement of molybdenum blue, an intensely-colored reduction product of phosphomolybdic acid. Methods have been devised for the specific production of this complex from various types of organic phosphate¹⁴.

The stability of phosphate groups towards acid or alkaline hydrolysis varies over a wide range¹⁵ and, as yet, detailed correlation

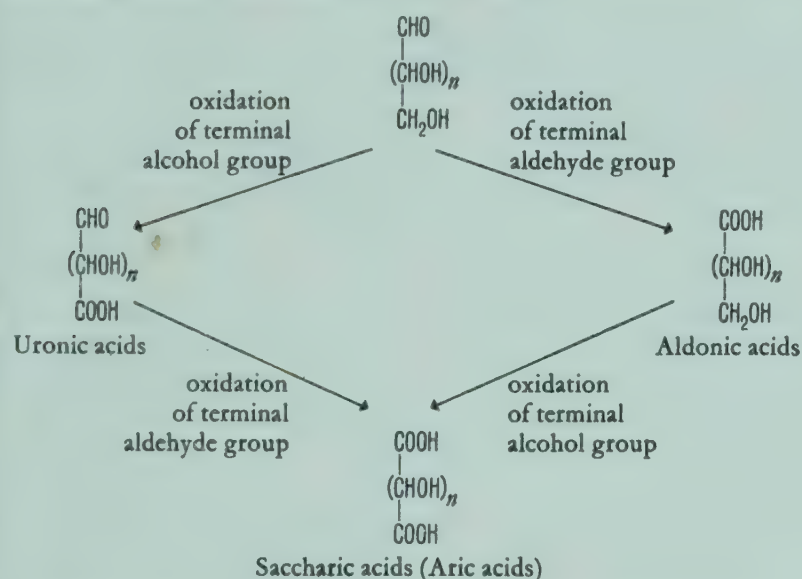
between the rates of hydrolysis and the position of the groups has not been made. Under conditions of acid or alkaline hydrolysis, migration of the phosphate group may occur, e.g. in the case of the phosphoglyceric acids¹⁶.

Polyhydric alcohols¹⁷

These compounds, which may be considered as reduction products of the monosaccharides, are of wide occurrence in plants but of limited occurrence in mammalian tissue. They are mostly crystalline compounds, generally possessing a sweet taste and devoid of any reducing properties. Those of importance to mammals are listed in Table 3 (page 439).

Primary oxidation products of carbohydrates

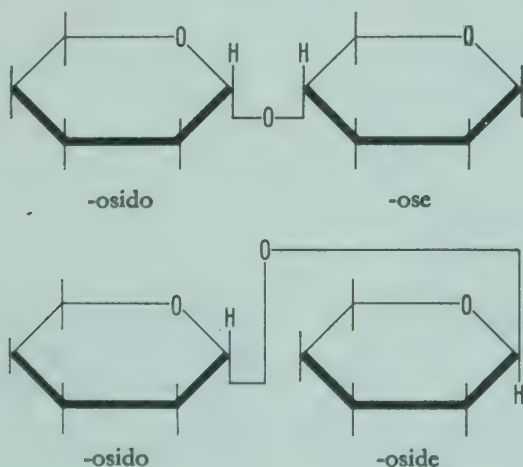
The nomenclature of the products of the oxidation of the terminal groups of aldoses is derived as follows:



Oxidation products of carbohydrates of importance to mammals are listed in Table 4 (page 440).

Oligosaccharides

Oligosaccharides are composed of monosaccharide molecules or their derivatives linked together through glycosidic linkages. The linkages may be glycosidic on one side only or on both sides. In the nomenclature of oligosaccharides, the sugar units in compounds of the former type are given the suffixes "-osido" and "-ose", while those in the latter type are indicated by "-osido" and "-oside". This is illustrated by the following scheme:



The term oligosaccharide is generally used to designate compounds containing between two and ten monosaccharide units per molecule. Oligosaccharides may be reducing or nonreducing, depending on the presence or absence of free hemiacetal hydroxyl groups.

The constituent monosaccharides are set free from an oligosaccharide by acid or enzymic hydrolysis.

The more important oligosaccharides of importance to mammals are given in Table 5 (page 441). A great variety of oligosaccharides is encountered in the plant kingdom.

Polysaccharides¹⁸

Polysaccharides, like oligosaccharides, are built up from a variety of monosaccharide units and their derivatives. They differ from oligosaccharides in that their molecules contain from ten up to several thousand monosaccharide units. The most commonly occurring constituent is D-glucose. However, D-mannose, D- and L-galactose, D-xylose, L-arabinose, uronic acids (D-glucuronic, D-galacturonic and D-mannuronic acids), amino-sugars (D-glucosamine, D-galactosamine, their N-acetyl derivatives and sulfate esters) are also found. In contrast with the oligosaccharides many of the polysaccharides are insoluble and nonreducing.

Their structure has been investigated by chemical methods¹⁹, e.g. by methylation and subsequent hydrolysis, by periodate oxidation, and by enzymic methods²⁰. The determination of the molecular size of polysaccharide molecules involves physical measurements of properties such as osmotic pressure, ultracentrifugation, viscosity and light scattering²⁰.

Polysaccharides may serve as:

- structural materials, e.g. cellulose (plants), chitin (insects and crustaceae), chondroitin sulfate (cartilage),
- food storage, e.g. glycogen (animals), starch (plants),
- lubricants in synovial fluids, constituents of special tissues (vitreous body of the eye; connective tissue), components of mucus, heparin, blood group substances²¹.

The principal polysaccharides of importance to mammals are listed in Table 6 (pages 442-44).

- For reviews see GILMAN et al. (Eds.), *Organic Chemistry: An Advanced Treatise*, vol. II, 2nd ed., New York, 1943, page 1532; PERCIVAL, E. G. V., *Structural Carbohydrate Chemistry*, London, 1950; PIGMAN, W. (Ed.), *The Carbohydrates*, New York, 1957.
- HONEYMAN, J., *An Introduction to the Chemistry of Carbohydrates*, Oxford, 1948.
- ROSANOFF, M. A., *J. Amer. chem. Soc.*, **28**, 114 (1906).
- BIJVOET, J. M., *Endeavour*, **14**, 71 (1955).
- HUDSON, C. S., *Advanc. Carbohydr. Chem.*, **3**, 1 (1948).
- MILLS, J. A., *Advanc. Carbohydr. Chem.*, **10**, 1 (1955).
- For reviews see KOWKABANY, G. N., *Advanc. Carbohydr. Chem.*, **9**, 303 (1954); HOUGH, L., in GLICK, D. (Ed.), *Methods of Biochemical Analysis*, vol. I, New York, 1954, page 205; ISHERWOOD, F. A., *Brit. med. Bull.*, **10**, 202 (1954); BLOCK et al., *A Manual of Paper Chromatography and Paper Electrophoresis*, New York, 1955.
- See DISCHE, Z., in GLICK, D. (Ed.), *Methods of Biochemical Analysis*, vol. II, New York, 1955, page 313.
- For comprehensive reviews of the chemistry of sugar phosphates see LELOIR, L. F., in ZECHMEISTER, L. (Ed.), *Fortschritte der Chemie organischer Naturstoffe*, vol. VIII, Vienna, 1951, page 47; FOSTER and OVEREND, *Quart. Rev. chem. Soc. Lond.*, **11**, 61 (1957).
- For a general account see AVISON and HAWKINS, *Quart. Rev. chem. Soc. Lond.*, **5**, 171 (1951).
- ISHERWOOD, F. A., *Brit. med. Bull.*, **10**, 202 (1954); BALSTON and TALBOT, *A Guide to Filter Paper and Cellulose Powder Chromatography*, London and Maidstone, 1952, page 60; BLOCK et al., *A Manual of Paper Chromatography and Paper Electrophoresis*, New York, 1955, page 144.
- LEDERER, M., *An Introduction to Paper Electrophoresis and Related Methods*, New York, 1955; BLOCK et al., *A Manual of Paper Chromatography and Paper Electrophoresis*, New York, 1955, page 333.
- COHN, W. E., in CHARGAFF and DAVIDSON (Eds.), *The Nucleic Acids*, vol. I, New York, 1955, page 211.
- LINDBERG and ERNSTER, in GLICK, D. (Ed.), *Methods of Biochemical Analysis*, vol. III, New York, 1956, page 1.
- See LELOIR, L. F., in ZECHMEISTER, L. (Ed.), *Fortschritte der Chemie organischer Naturstoffe*, vol. VIII, Vienna, 1951, page 47.
- See BALLOU and FISCHER, *J. Amer. chem. Soc.*, **76**, 3188 (1954).
- For a review see LOHMAR, R. L., in PIGMAN, W. (Ed.), *The Carbohydrates*, New York, 1957, page 241.
- For reviews see WHISTLER and SMART, *Polysaccharide Chemistry*, New York, 1953; WHISTLER and MCGILVRAY, *Ann. Rev. Biochem.*, **23**, 79 (1954); ASPINALL and SCHWARZ, *Ann. Rep. Progr. Chem.*, **52**, 255 (1955).
- MANNERS, D. J., *Quart. Rev. chem. Soc. Lond.*, **9**, 73 (1955).
- GREENWOOD, C. T., *Advanc. Carbohydr. Chem.*, **7**, 289 (1952).
- Cf. KENT and WHITEHOUSE, *Biochemistry of the Aminosugars*, London, 1955.

Table 1 Monosaccharides of importance to mammals

Some of the more important sugars which are constituents of substances of medical interest are also included in this table

Name	Formula and mol. wt.	Structure	Specific rotation	Occurrence
<i>Trioses</i>				
D-Glyceraldehyde (2,3-dihydroxypropanal)	C ₃ H ₆ O ₃ 90.08	$\begin{array}{c} \text{CHO} \\ \\ \text{HCOH} \\ \\ \text{CH}_2\text{OH} \end{array}$	$[\alpha]_D^{20} + 13.5^\circ$	As phosphate ester (see Table 2, page 435)
D-Dihydroxyacetone (1:3-dihydroxypropan-2-one, oxantin)	C ₃ H ₆ O ₃ 90.08	$\begin{array}{ccc} \text{CH}_2\text{OH} & & \text{CH}_2\text{OH} \\ & \text{or} & \\ \text{CO} & & \text{C(OH)} \\ & & \\ \text{CH}_2\text{OH} & & \text{CHOH} \end{array}$	(inactive)	As phosphate ester (see Table 2, page 435)
<i>Tetroses</i>				
D-Erythrose	C ₄ H ₈ O ₄ 120.11		$[\alpha]_D^{20} - 14.8^\circ$	As phosphate ester (see Table 2, page 435)
L-Erythrulose	C ₄ H ₈ O ₄ 120.11	$\begin{array}{c} \text{CH}_2\text{OH} \\ \\ \text{CO} \\ \\ \text{HOCH} \\ \\ \text{CH}_2\text{OH} \end{array}$	$[\alpha]_D^{20} + 12^\circ$	As metabolically active phosphate ester (see Table 2, page 435)
2-Desoxy-D-ribose (2-desoxy-D-erythro-pentose, thyminose, desoxyarabinose)	C ₅ H ₁₀ O ₄ 134.14		$[\alpha]_D^{25} - 50^\circ$	Universal occurrence as constituent of nucleosides, nucleotides and nucleic acids. For phosphates see Table 2, page 436
D-Digitoxose (2-desoxy-D-altro-methylose)	C ₆ H ₁₂ O ₄ 148.16		$[\alpha]_D^{20} + 46.5^\circ$	Component of digitalis glycosides
<i>Pentoses</i>				
β-D-Arabinose	C ₅ H ₁₀ O ₅ 150.14		$[\alpha]_D^{20} - 105^\circ$	In glycosides of aloe and tubercle bacilli
DL-Arabinose	C ₅ H ₁₀ O ₅ 150.14	– (equimolecular mixture of D- and L-arabinoses)	(inactive)	Isolated from urine in pentosuria (rare case of metabolic formation of a racemate)
L-Fucose (6-desoxy-L-galactose)	C ₆ H ₁₂ O ₅ 164.16		$[\alpha]_D^{20} - 153^\circ \rightarrow + 76^\circ$	Component of polysaccharides of human milk, blood-group substances, marine algae, gum tragacanth
L-Rhamnose (6-desoxy-L-mannose, isodulcitol)	C ₆ H ₁₂ O ₅ 164.16		α-form, 1 H ₂ O: $[\alpha]_D^{20} - 9^\circ$ β-form: $[\alpha]_D + 38^\circ$	As glycoside in plant pigments, gums and mucilages. Common component of cardiac glycosides

Table 1 Monosaccharides of importance to mammals (continued)

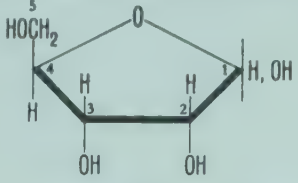
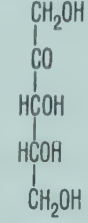

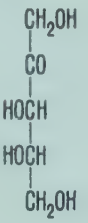
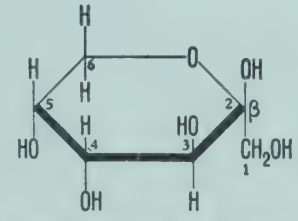
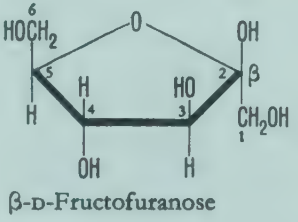
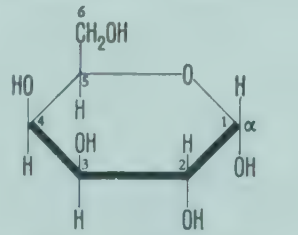
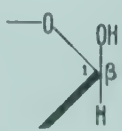
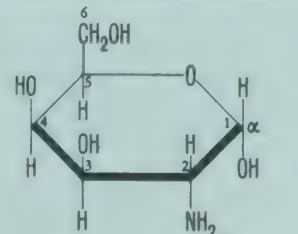
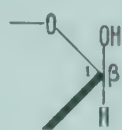
Name	Formula and mol. wt.	Structure	Specific rotation	Occurrence
D-Ribose (D-ribofuranose)	$C_5H_{10}O_5$ 150.14		$[\alpha]_D^{20} - 23.7^\circ$ (4% soln.)	Universal occurrence as constituent of nucleosides, nucleotides and nucleic acids. For phosphates see Table 2, pages 435–436
D-Ribulose (D-erythro-pentulose, D-adonose, D-arabulose)	$C_5H_{10}O_5$ 150.14			As phosphate esters (see Table 2, page 436). Intermediary metabolite in glucose oxidation
D-Xylulose (L-threo-pentulose, D-xyloketose, D-lyxulose, D-lyxoketose)	$C_5H_{10}O_5$ 150.14		$[\alpha]_D^{20} - 33^\circ$	As phosphate ester (see Table 2, page 436)
L-Xylulose (L-xyloketose, L-lyxulose, L-lyxoketose)	$C_5H_{10}O_5$ 150.14		$[\alpha]_D^{20} + 33^\circ$	In urine in pentosuria
<i>Hexoses</i>				
D-Fructose (2-keto-D-arabohexose, levulose, fruit sugar)	$C_6H_{12}O_6$ 180.16	 β -D-Fructopyranose  β -D-Fructofuranose	β -form: $[\alpha]_D^{20} - 133.5^\circ \rightarrow -92^\circ$	As phosphate esters (see Table 2, page 436). Component of many polysaccharides (combined with glucose in sucrose). Has pyranose form when crystalline, but furanose form in all natural products. Sweetest of all known sugars
D-Galactose (cerebrose, brain sugar)	$C_6H_{12}O_6$ 180.16	 α -D-Galactopyranose  β -D-Galactopyranose	α -form: $[\alpha]_D^{20} + 144^\circ \rightarrow +80.5^\circ$ β -form: $[\alpha]_D^{20} + 54^\circ \rightarrow +80.5^\circ$	Present in mammalian tissues as phosphate ester (see Table 2, page 437). Component of cerebroside and gangliosides, and of polysaccharides both as sugar and derived amino sugar (e.g. lactose, raffinose, stachyose)
D-Galactosamine (D-chondrosamine, 2-amino-2-desoxy-D-galactose)	$C_6H_{13}O_5N$ 179.18	 α -D-Galactosamine  β -D-Galactosamine	α -form, 1 HCl: $[\alpha]_D^{20} + 135^\circ \rightarrow +93^\circ$ β -form, 1 HCl: $[\alpha]_D^{20} + 39^\circ \rightarrow +93^\circ$	Widely distributed in nature as component of mucopolysaccharides, cartilage, tendons (chondroitin), β -heparin, lipoids, cerebral gangliosides, blood-group substances

Table 1 Monosaccharides of importance to mammals (concluded)

Name	Formula and mol. wt.	Structure	Specific rotation	Occurrence
N-Acetyl-D-galactosamine	$C_6H_{15}O_6N$ 221.22		$[\alpha]_D^{20} + 115^\circ \rightarrow + 80^\circ$	Form in which D-galactosamine (see below) occurs as component of chondroitin, etc.
D-Glucose (dextrose, blood sugar, grape sugar, corn sugar)	$C_6H_{12}O_6$ 180.16		α -form: $[\alpha]_D^{20} + 113.4^\circ \rightarrow + 52.5^\circ$ β -form: $[\alpha]_D^{20} + 19.3^\circ \rightarrow + 52.5^\circ$	As phosphate esters (see Table 2, page 437). Most widely distributed of all sugars. Found free in many biological fluids, e.g. blood, lymph, cerebrospinal fluid. Component of polysaccharides both as sugar and amino sugar (see Glucosamine, below)
D-Glucosamine (chitosamine, 2-amino-2-desoxy-D-glucose)	$C_6H_{13}O_5N$ 179.18		α -form: $[\alpha]_D^{20} + 100^\circ \rightarrow + 47.5^\circ$ β -form: $[\alpha]_D^{20} + 14^\circ \rightarrow + 47.5^\circ$	Component (as N-acetylglucosamine, see below) of chitin, heparin, hyaluronic acid, blood-group polysaccharides, oligosaccharides of human milk
N-Acetyl-D-glucosamine	$C_8H_{15}O_6N$ 221.22			Sole component of chitin; component of heparin, hyaluronic acid, blood-group polysaccharides, oligosaccharides of human milk
N-Methyl-L-glucosamine	$C_7H_{15}O_5N$ 193.21			Component of streptomycin
D-Mannose (seminose)	$C_6H_{12}O_6$ 180.16		α -form: $[\alpha]_D^{20} + 29.9^\circ \rightarrow + 14.5^\circ$ β -form: $[\alpha]_D^{20} - 16.3^\circ \rightarrow + 14.5^\circ$	As phosphate ester (see Table 2, page 437). Widely distributed as component of mannans and hemicelluloses. Limited occurrence as component of glycoproteins.
Heptose				
D-Sedoheptulose (D-altra-ketoheptose, D-altra-heptulose)	$C_7H_{14}O_7$ 210.19		$[\alpha]_D^{20} + 2-3^\circ$ Ba salt: $[\alpha]_{400}^{20} + 8^\circ$	As phosphate ester (see Table 2, page 438)

Table 2 Sugar phosphates of importance to mammals

(Not including nucleotides, for which see Tables 10c, 11 and 12, pages 458–466)

Name	Formula and mol. wt.	Structure	Elementary composition			Specific rotation	Biological function	Reference*
			C	H	P			
Dihydroxyacetone phosphate	$C_3H_7O_6P$ 170.06	$\begin{array}{c} CH_2OH \\ \\ CO \\ \\ CH_2OPO_3H_2 \end{array}$	21.19	4.15	18.22		Intermediate of glycolysis	1
D-Glyceraldehyde 3-phosphate ("FISCHER-BAER Ester")	$C_3H_7O_6P$ 170.06	$\begin{array}{c} CHO \\ \\ HCOH \\ \\ CH_2OPO_3H_2 \end{array}$	21.19	4.15	18.22	$[\alpha]_D^{20} + 14^\circ$	Intermediate of glycolysis	2
L-Glycerol 1-phosphate	$C_3H_8O_6P$ 172.08	$\begin{array}{c} CH_2OPO_3H_2 \\ \\ HOCH \\ \\ CH_2OH \end{array}$	20.94	5.27	18.00	$[\alpha]_D^{20} - 1.45^\circ$ (Ba salt)	Intermediate of fat metabolism. Component of phospholipids	3
D-Glyceric acid 2-phosphate ("KIESSLING Ester")	$C_3H_7O_7P$ 186.06	$\begin{array}{c} COOH \\ \\ HCOPO_3H_2 \\ \\ CH_2OH \end{array}$	19.36	3.79	16.65	$[\alpha]_D^{20} + 13^\circ$ (N HCl)	Intermediate of glycolysis	4
D-Glyceric acid 3-phosphate	$C_3H_7O_7P$ 186.06	$\begin{array}{c} COOH \\ \\ HCOH \\ \\ CH_2OPO_3H_2 \end{array}$	19.36	3.79	16.65	$[\alpha]_D^{20} - 14.5^\circ$ (N HCl)	Intermediate of glycolysis	5
D-Glyceric acid 1,3-diphosphate	$C_3H_8O_{10}P_2$ 266.05	$\begin{array}{c} COOPO_3H_2 \\ \\ HCOH \\ \\ CH_2OPO_3H_2 \end{array}$	13.55	3.03	23.30	$[\alpha]_D^{20} - 2.3^\circ$	Intermediate of glycolysis	6
D-Glyceric acid 2,3-diphosphate	$C_3H_8O_{10}P_2$ 266.05	$\begin{array}{c} COOH \\ \\ HCOPO_3H_2 \\ \\ CH_2OPO_3H_2 \end{array}$	13.55	3.03	23.30	$[\alpha]_D^{20} - 2.3^\circ$	Intermediate of glycolysis	7
Pyruvic acid enol phosphate (phosphopyruvic acid)	$C_3H_5O_6P$ 168.05	$\begin{array}{c} COOH \\ \\ COPO_3H_2 \\ \\ CH_2 \end{array}$	21.44	2.99	18.43		Intermediate of glycolysis	8
D-Erythrose-4-phosphate	$C_4H_9O_7P$ 200.09	$\begin{array}{c} CHO \\ \\ HCOH \\ \\ HCOH \\ \\ CH_2OPO_3H_2 \end{array}$	24.01	4.53	15.49		Intermediate of pentose-phosphate cycle	9
L-Erythrulose-1-phosphate	$C_4H_9O_7P$ 200.09	$\begin{array}{c} CH_2OPO_3H_2 \\ \\ CO \\ \\ HOCH \\ \\ CH_2OH \end{array}$	24.01	4.53	15.49		Function not known	10
α -D-Ribose-1-phosphate (furanose form)	$C_5H_{11}O_8P$ 230.12		26.15	4.83	13.49		Intermediate of nucleotide metabolism	11
D-Ribose-5-phosphate (furanose form)	$C_5H_{11}O_8P$ 230.12		26.15	4.83	13.49	$[\alpha]_D^{20} + 16.5^\circ$	Intermediate of pentose-phosphate cycle and nucleotide synthesis	12

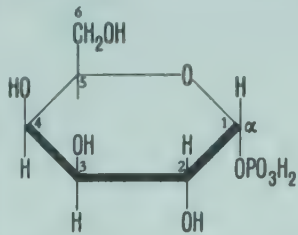
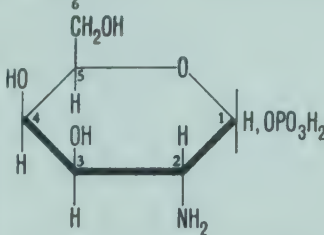
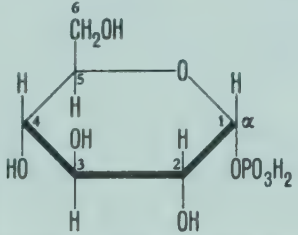
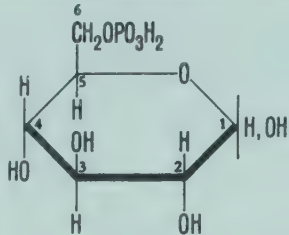
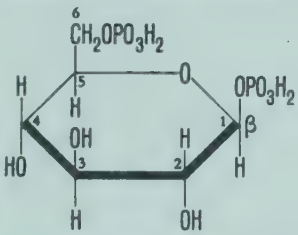
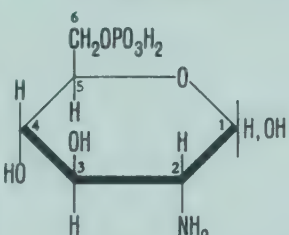
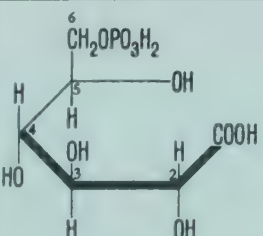
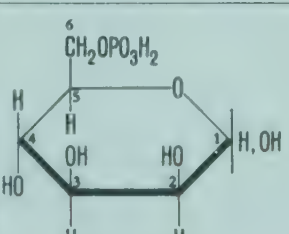
* See end of table, page 438.

Table 2 Sugar phosphates of importance to mammals (continued)

Name	Formula and mol. wt.	Structure	Elementary composition			Specific rotation	Biological function	Reference*
			C	H	P			
D-Ribose-1,5-diphosphate (furanose form)	C ₅ H ₁₃ O ₁₁ P ₂ 310.10		19.37	3.90	25.15		Intermediate of interconversion of ribose-1-phosphate and ribose-5-phosphate	13
D-Ribose-5-phosphate-1-pyrophosphate (5-phosphoribosyl-1-pyrophosphate)	C ₅ H ₁₃ O ₁₄ P ₃ 390.08		15.40	3.36	23.83		Intermediate of nucleotide synthesis	14
Desoxyribose-1-phosphate (furanose form)	C ₅ H ₁₁ O ₇ P 214.12		28.05	5.18	14.47		Product of nucleoside degradation	15
Desoxyribose-5-phosphate (furanose form)	C ₅ H ₁₁ O ₇ P 214.12		28.05	5.18	14.47		Component of desoxynucleic acids and desoxynucleotides	
D-Ribulose-5-phosphate	C ₅ H ₁₁ O ₈ P 230.12		26.15	4.83	13.49	[α] _D ²⁰ − 40°	Intermediate of pentose-phosphate cycle	16
D-Xylulose-5-phosphate	C ₅ H ₁₁ O ₈ P 230.12		26.15	4.83	13.49		Intermediate of pentose-phosphate cycle	16
D-Fructose-1-phosphate (pyranose form) ("ROBISON-TANKO Ester")	C ₆ H ₁₃ O ₈ P 260.15		27.70	5.04	11.91	[α] _D ²⁰ − 56°	Intermediate of glycolysis	17
D-Fructose-6-phosphate (furanose form) ("NEUBERG Ester")	C ₆ H ₁₃ O ₈ P 260.15		27.70	5.04	11.91	[α] _D ¹⁹ + 3.58° (Ba salt)	Intermediate of glycolysis	18
D-Fructose-1,6-diphosphate (furanose form) ("HARDEN-YOUNG Ester")	C ₆ H ₁₄ O ₁₂ P ₂ 340.13		21.19	4.15	18.22	[α] _D ¹⁷ + 4.1°	Intermediate of glycolysis	18

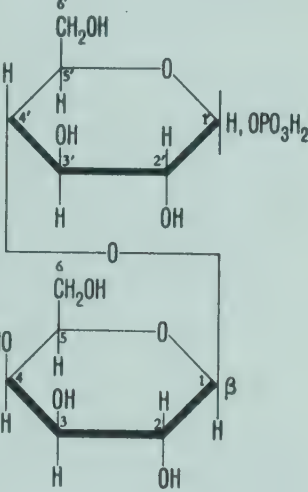
* See end of table, page 438.

Table 2 Sugar phosphates of importance to mammals (continued)

Name	Formula and mol. wt.	Structure	Elementary composition			Specific rotation	Biological function	Reference*
			C	H	P			
α -D-Galactose-1-phosphate (pyranose form)	$C_6H_{13}O_8P$ 260.15		27.70	5.04	11.91	$[\alpha]_D^{18} + 148.5^\circ$	Intermediate of galactose metabolism	19
D-Galactosamine-1-phosphate	$C_6H_{14}O_8NP$ 259.16		27.81	5.45	11.51		Formed from galactosamine in brain tissue extracts and <i>Saccharomyces fragilis</i>	20
α -D-Glucose-1-phosphate (pyranose form) ("CORI Ester")	$C_6H_{13}O_8P$ 260.15		27.70	5.04	11.91	$[\alpha]_D^{25} + 120^\circ$	Intermediate of glucose-glycogen interconversion	21
D-Glucose-6-phosphate (pyranose form) ("ROBISON Ester")	$C_6H_{13}O_8P$ 260.15		27.70	5.04	11.91	$[\alpha]_D^{25} + 34.2^\circ$	Intermediate of glycolysis	22
β -D-Glucose-1,6-diphosphate (pyranose form)	$C_6H_{14}O_{12}P_2$ 340.13		21.19	4.15	18.22	$[\alpha]_D^{20} - 19^\circ$ (pH 8)	Intermediate of glucose-glycogen interconversion	23
D-Glucosamine-6-phosphate	$C_6H_{14}O_8NP$ 259.16		27.81	5.45	11.51	$[\alpha]_D^{20} + 48.5^\circ$	Formed from D-glucosamine by yeast enzyme preparations and by hexokinase	24
D-Gluconic acid 6-phosphate	$C_6H_{13}O_{10}P$ 276.15		26.10	4.74	11.22	$[\alpha]_{5461}^{20} + 0.2^\circ$	Intermediate of pentose-phosphate cycle	25
D-Mannose-6-phosphate (pyranose form)	$C_6H_{13}O_8P$ 260.15		27.70	5.04	11.91	$[\alpha]_{5461}^{20} + 15.1^\circ$	Intermediate of mannose metabolism	26

* See end of table, page 438.

Table 2 Sugar phosphates of importance to mammals (concluded)

Name	Formula and mol. wt.	Structure	Elementary composition			Specific rotation	Biological function	Reference (see below)
			C	H	P			
D-Sedoheptulose-7-phosphate	C ₇ H ₁₅ O ₁₀ P 290.17	$\begin{array}{c} \text{CH}_2\text{OH} \\ \\ \text{CO} \\ \\ \text{HOCH} \\ \\ \text{HCOH} \\ \\ \text{HCOH} \\ \\ \text{HCOH} \\ \\ \text{CH}_2\text{OPO}_3\text{H}_2 \end{array}$	28.97	5.21	10.68		Intermediate of pentose-phosphate cycle	27
D-Sedoheptulose-1,7-diphosphate	C ₇ H ₁₃ O ₁₃ P ₂ 370.16	$\begin{array}{c} \text{CH}_2\text{OPO}_3\text{H}_2 \\ \\ \text{CO} \\ \\ \text{HOCH} \\ \\ \text{HCOH} \\ \\ \text{HCOH} \\ \\ \text{HCOH} \\ \\ \text{CH}_2\text{OPO}_3\text{H}_2 \end{array}$	22.72	4.36	16.74		Intermediate of pentose-phosphate cycle	28
Lactose-phosphate	C ₁₂ H ₂₃ O ₁₄ P 422.29	 (probable structure)	34.13	5.49	7.34	[α] _D ²⁵ +99.5°	Possible intermediate in lactose synthesis	29

References

1) BALLOU and FISCHER, *J. Amer. chem. Soc.*, **78**, 1659 (1956) 2) MEYERHOF, O., *Bull. Soc. Chim. biol. (Paris)*, **20**, 1033, 1345 (1938); BALLOU and FISCHER, *J. Amer. chem. Soc.*, **77**, 3329 (1955). 3) BAER and FISCHER, *J. biol. Chem.*, **128**, 491 (1939); BAER and FISCHER, in BALL, E. G. (Ed.), *Biochemical Preparations*, vol. II, New York, 1952, page 31. 4) KIESSLING, W., *Ber. dtsh. chem. Ges.*, **68**, 243 (1935); BALLOU and FISCHER, *J. Amer. chem. Soc.*, **76**, 3188 (1954). 5) NEUBERG and LUSTIG, *Arch. Biochem.*, **1**, 311 (1942); BALLOU and FISCHER, *Abstr. Amer. chem. Soc. 126th Meeting*, 1954, page 7D. 6) NEGELEIN and BRÖMEL, *Biochem. Z.*, **301**, 135 (1939). 7) BAER, E., *J. biol. Chem.*, **185**, 763 (1950). 8) LOHMANN and MEYERHOF, *Biochem. Z.*, **273**, 60 (1934); BAER and FISCHER, *J. biol. Chem.*, **180**, 145 (1949); BAER and FISCHER, in BALL, E. G. (Ed.), *Biochemical Preparations*, vol. II, New York, 1952, page 25. 9) BALLOU et al., *J. Amer. chem. Soc.*, **77**, 2658 (1955). 10) CHARALAMPOUS, F. C., *J. biol. Chem.*, **211**, 249 (1954). 11) KALCKAR, H. M., *J. biol. Chem.*, **167**, 477 (1947); WRIGHT and KHORANA, *J. Amer. chem. Soc.*, **78**, 811 (1956). 12) LOLOIR, L. F., in ZECHMEISTER, L. (Ed.), *Fortschritte der Chemie organischer Naturstoffe*, vol. VIII, Vienna, 1951, page 70. 13) KLENOW, H., *Arch. Biochem.*, **46**, 186 (1953). 14) KORNBERG et al., *J. biol. Chem.*, **215**, 389 (1955). 15) FRIEDKIN, M., *J. biol. Chem.*, **184**, 449 (1950). 16) DICKENS and WILLIAMSON, *Nature*, **176**, 400 (1955). 17) TANKO and ROBISON, *Biochem. J.*, **29**, 961 (1935); BRIGL and MÜLLER, *Ber. dtsh. chem. Ges.*, **72**, 2121 (1939). 18) NEUBERG et al., *Arch. Biochem.*, **3**, 33 (1944); TANKO, B., *Abstracts of the Communications of the 1st International Congress of Biochemistry*, Cambridge, 1949, page 222. 19) KOSTERLITZ, H. W., *Biochem. J.*, **37**, 318 (1943). 20) CARDINI and LOLOIR, *Arch. Biochem. Biophys.*, **45**, 55 (1953). 21) CORI et al., *J. biol. Chem.*, **121**, 465 (1937); WOLFROM and PLETCHER, *J. Amer. chem. Soc.*, **63**, 1050 (1941); KRAHL and CORI, in CARTER, H. E. (Ed.), *Biochemical Preparations*, vol. I, New York, 1949, page 33. 22) LOLOIR, L. F., in ZECHMEISTER, L. (Ed.), *Fortschritte der Chemie organischer Naturstoffe*, vol. VIII, Vienna, 1951, page 76. 23) CARDINI et al., *Arch. Biochem.*, **22**, 87 (1949); POSTERNAK, T., *J. biol. Chem.*, **180**, 1269 (1949). 24) KENT and WHITEHOUSE, *Biochemistry of the Aminosugars*, London, 1955, page 31. 25) ROBISON and KING, *Biochem. J.*, **25**, 323 (1931). 26) ROBISON, R., *Biochem. J.*, **26**, 2191 (1932); SLEIN, M. W., *J. biol. Chem.*, **186**, 753 (1950). 27) HORECKER and SMYRNIOTIS, *J. biol. Chem.*, **212**, 811 (1955). 28) HORECKER et al., *J. biol. Chem.*, **212**, 827 (1955). 29) MCGEOWN and MALPRESS, *Biochem. J.*, **52**, 606 (1952); GANDER et al., *Arch. Biochem. Biophys.*, **60**, 259 (1956).

Table 3 Polyhydric alcohols of importance to mammals

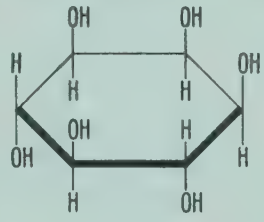
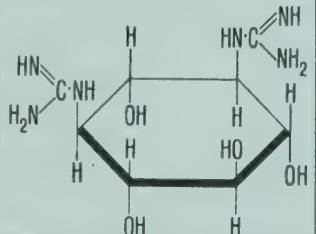
Name	Formula and mol. wt.	Structure	Specific rotation	Occurrence
Glycerol	$C_3H_8O_3$ 92.10	$\begin{array}{c} CH_2OH \\ \\ HCOH \\ \\ CH_2OH \end{array}$		Wide occurrence in lipids of mammalian tissues. Sweet taste
Ribitol (adonitol)	$C_5H_{12}O_5$ 152.15	$\begin{array}{c} CH_2OH \\ \\ HCOH \\ \\ HCOH \\ \\ HCOH \\ \\ CH_2OH \end{array}$		Component of riboflavin (vitamin B_2 , see page 215). Also found in <i>Adonis vernalis</i>
<i>myo</i> -Inositol ("mesoInositol")	$C_6H_{12}O_6$ 180.16		(inactive)	Widely distributed in plant and animal kingdoms. Found both free and combined in muscle, heart, liver and other tissues. Component of brain cephalin. The hexaphosphate (phytin) is the organic phosphorus reserve material of green plants
Streptidine	$C_8H_{18}O_4N_6$ 262.28			Component of streptomycin

Table 4 Oxidation products of carbohydrates

Name	Formula and mol. wt.	Structure	Specific rotation	Occurrence
<i>Aldonic acids</i>				
D-Glyceric acid (D- α,β -dihydroxypropionic acid)	C ₃ H ₆ O ₄ 106.08			As phosphate esters (see Table 2, page 435) which are intermediates in glycolysis
L-Ascorbic acid (L-xyloascorbic acid, vitamin C)	C ₆ H ₈ O ₆ 176.13		$[\alpha]_D^{20} + 49^\circ$	See under Vitamins, page 213
D-Gluconic acid (dextronic acid)	C ₆ H ₁₂ O ₇ 196.16		$[\alpha]_D^{20} - 6.7^\circ \rightarrow + 17.5^\circ$	As phosphate ester (see Table 2, page 437), intermediate in pentose-phosphate cycle (see page 499)
<i>Uronic acids</i>				
α -D-Galacturonic acid	C ₆ H ₁₂ O ₇ 196.16		$[\alpha]_D^{21} + 100^\circ \rightarrow + 68^\circ$	Main component of pectins. Also occurs in some plant gums and mucilages and bacterial polysaccharides
β -D-Glucuronic acid	C ₆ H ₁₂ O ₇ 196.16		$[\alpha]_D^{20} + 12^\circ \rightarrow + 36^\circ$	Component of mucopolysaccharides ¹ . Many aliphatic and aromatic hydroxy compounds and acids are excreted as glucuronides ² . Has pyranose form in natural products (see also page 501)
D-Iduronic acid	C ₆ H ₁₂ O ₇ 196.16			Component of chondroitin sulfate B ³

1) Cf. KENT and WHITEHOUSE, *Biochemistry of the Aminosugars*, London, 1955. 2) TEAGUE, R. S., *Advanc. Carbohydr. Chem.*, **9**, 185 (1954); WILLIAMS, R. T., *Detoxication Mechanisms*, London, 1947. 3) HOFFMAN et al., *Science*, **124**, 1252 (1956).

Table 5 Oligosaccharides of importance to mammals

Name	Formula and mol. wt.	Structure	Specific rotation	Remarks
<p>Cellulobiose (4'-[β-D-glucopyranosido]-β-D-glucopyranose)</p>	<p>$C_{12}H_{22}O_{11}$ 342.31</p>	<p>Disaccharides</p>	<p>$[\alpha]_D^{20} + 14.2^\circ \rightarrow + 34.6^\circ$</p>	<p>Breakdown product of cellulose arising in herbivores in the course of digestion. Component also of lichenin</p>
<p>Lactose (4'-[β-D-galactopyranosido]-β-D-glucopyranose)</p>	<p>$C_{12}H_{22}O_{11}$ 342.31</p>		<p>α-form, 1 H₂O: $[\alpha]_D^{20} + 85^\circ \rightarrow + 52.6^\circ$ β-form: $[\alpha]_D^{20} + 34.9^\circ \rightarrow + 55.4^\circ$</p>	<p>Constituent of mammalian milk (4-8%)*. Only faintly sweet</p>
<p>Maltose (4'-[α-D-glucopyranosido]-β-D-glucopyranose)</p>	<p>$C_{12}H_{22}O_{11}$ 342.31</p>		<p>β-form, 1 H₂O: $[\alpha]_D^{20} + 111.7^\circ \rightarrow + 130.4^\circ$</p>	<p>Breakdown product of starch and glycogen, arising in the course of digestion. Found free in some plants (barley) and in honey</p>
<p>Sucrose (saccharose, canesugar, beet sugar, α-D-glucopyranosido-β-D-fructofuranoside)</p>	<p>$C_{12}H_{22}O_{11}$ 342.31</p>		<p>$[\alpha]_D^{20} + 66.53^\circ$</p>	<p>Almost universal occurrence in vegetable kingdom</p>
<p>Fucosidolactose (2-[α-L-fucopyranosido]lactose)</p>	<p>$C_{18}H_{30}O_{13}$ 486.44</p>	<p>Trisaccharide</p>		<p>Occurs in traces in human milk*</p>

* For other oligosaccharides isolated from human milk see BELL et al., *Ann. Rep. Progr. Chem.*, **52**, 333 (1955); KUNN, R., *Bull. Soc. Chim. biol. (Paris)*, **40**, 297 (1958).

Table 6 Polysaccharides of importance to mammals (For references see page 444.)

Name	Formula and mol. wt.	Structure	Specific rotation	Remarks
Amylopectin ¹ (α -amylose, B-fraction of starch)	Up to 52×10^6 for potato amylopectin ²	Highly-branched molecule composed of several hundred unit-chains, each of which comprises 20–26 α -1:4-linked glucose residues; the unit-chains are inter linked by glycosidic bonds from the reducing group to C-6 of a glucose residue in an adjacent chain: 	$[\alpha]_D^{20} + 150^\circ$	Main constituent of starches (usually ca. 80%). Has been synthesized by incubation of glucose-1-phosphate with Q-enzyme of potato juice in presence of potato phosphorylase ³
Amylose ¹ (β -amylose, A-fraction of starch)	$(323)_n$, up to 1×10^6	Essentially a linear chain of α -1:4-linked glucose residues: 	$[\alpha]_D^{20} + 220^\circ$	Constituent of starch (ca. 20%). Absent in some starches, e.g. that of “waxy” maize (corn). Has been synthesized by incubation of glucose-1-phosphate with potato phosphorylase ⁴
Cellulose	$(323)_n$, up to 1.7×10^6	Linear chain of β -1:4-linked glucose residues: 		Chief structural polysaccharide of plants. Also found in algae, bacterial membranes, and as tunicin in some lower animals. Not digested by man
Chitin	$(203, 19)_n$, ca. 4×10^5	Linear chain of β -1:4-linked N-acetyl-D-glucosamine residues: 	$[\alpha]_D^{20} - 14.7^\circ$ (in HCl)	Skeletal substance of molluscs and insects. Also found in lower plants and fungi

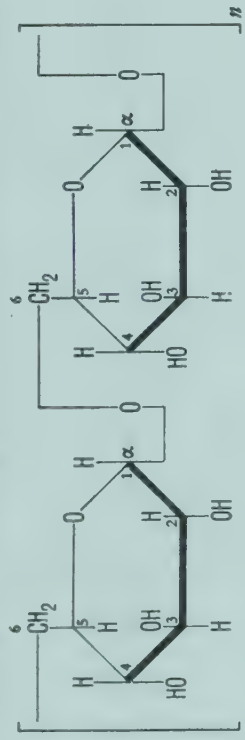
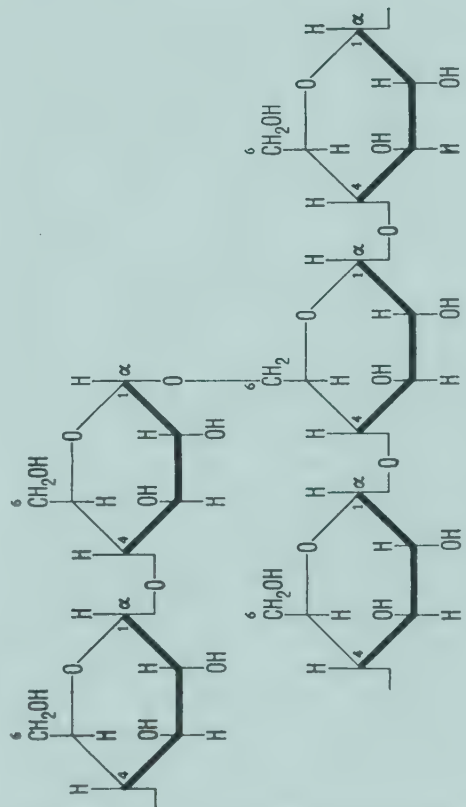
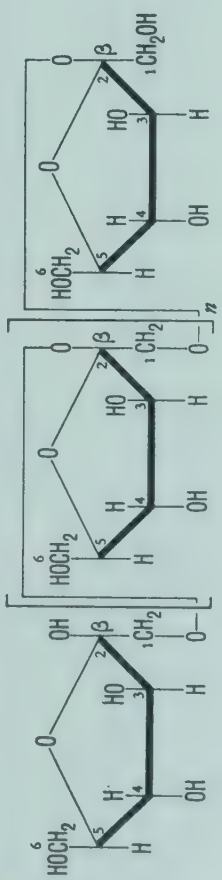
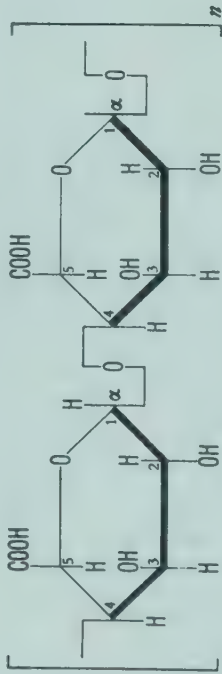
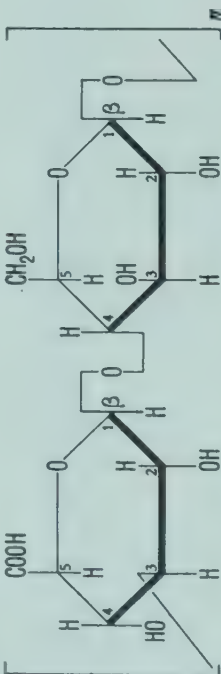
Chondroitin sulfate	Highly polydisperse; minimum ca. 26,000 ⁵	Polymer composed of D-glucuronic acid, D-glucosamine, N-acetyl-D-galactosamine and sulfate residues. Detailed structure not established ⁶	Present in most mammalian cartilaginous tissue
Dextran ⁷	(323) _n , ca. 4 × 10 ⁵	Probably α-1:6-linked glucose residues in branched or straight chains, e. g. 	Produced extracellularly by bacteria, e.g. <i>Leuconostoc mesenteroides</i> . Partially degraded dextrans are used as blood-plasma substitutes ⁸
Glycogen (liver starch)	Polydisperse; for most glycogens at least 2 × 10 ⁶	Highly-branched molecule resembling amylopectin and consisting of unit chains of α-1:4-linked glucose residues interlinked by α-1:6-glucosidic bonds. ¹⁰ 	Reserve carbohydrate of animal tissues. Converted in muscle to lactic acid during glycolysis (see page 473). Also present in yeast. Has been synthesized by action of heart or liver phosphorylase on glucose-1-phosphate ⁹
Heparin	ca. 17,000 ¹¹	Polymer composed of D-glucosamine, D-glucuronic acid, acetate and sulfate residues. Detailed structure not established ⁶	Occurs in animal tissue. Blood anti-coagulant
Hyaluronic acid	ca. 1 × 10 ⁶ ¹²	Polymer composed of D-glucosamine, D-glucuronic acid, and acetate residues. Detailed structure not established ⁴	Widely distributed in tissues and inter-cellular fluids

Table 6 Polysaccharides of importance to mammals (concluded)

Name	Formula and mol. wt.	Structure	Specific rotation	Remarks
Inulin	$(162.14)_n$, ca. 5000	Linear chain of about 30 β -1:2-linked fructofuranose units: 	$[\alpha]_D^{20} - 40^\circ$	Reserve carbohydrate of many plants, alone or with starch
Pectic acid (pectins)	$(346)_n$, up to 5×10^4	Probably a linear chain of α -1:4-linked D-galacturonic acid residues: ¹³ 	$[\alpha]_D^{20}$ ca. $+ 240^\circ$	Important cell-wall constituent of plants. Occurs as Ca salt or methyl ester
Pneumococcal polysaccharides Type 3	1.4×10^5	Alternating glucose and glucuronic acid residues, probably linked 1:3 and 1:4 respectively: ¹⁴ 		An example of the 40 odd pneumococcal polysaccharides known, many of unknown structure. Responsible for type specificity of pneumococci. Effective as antigen
Starches (amylum)	Highly poly-disperse	Consist mainly of mixtures of amylose and amylopectin (see above in this Table) in proportion 20:80. Some starches contain no amylose		Reserve carbohydrates of many plants

References

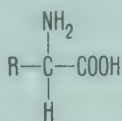
1) For reviews of starch chemistry see BOURNE, E. J., *Chem. and Ind.*, 1951, 1047; MEYER and GIBBONS, *Advanc. Enzymol.*, 12, 341 (1951).
2) WITNAUER et al., *J. chem. Phys.*, 20, 1978 (1952). 3) BOURNE and PEAT, *J. chem. Soc.*, 1945, 877; BARKER et al., *ibid.*, 1949, 1705, 1712. 4) HANES,

C. S., *Proc. roy. Soc. B*, 128, 421 (1940); 129, 174 (1940). 5) BLIX and SNELL-MAN, *Ark. Kemi Mineral. Geol.*, 19A, No. 32 (1945). 6) JEANLOZ, R. W., *Proceedings of the Third International Congress of Biochemistry, Brussels 1955*, New York, 1956, page 65. 7) STACEY and RICKETS, in ZECHMEISTER, L. (Ed.), *Fortschritte der Chemie organischer Naturstoffe*, vol. VIII, Vienna, 1951, page 28. 8) MANNERS, D. J., *Quart. Rev. chem. Soc. Lond.*, 9, 88 (1955).

9) BEAR and CORI, *J. biol. Chem.*, 140, 111 (1941). 10) BELL and MANNERS, *J. chem. Soc. Lond.*, 1954, 1891. 11) JENSEN et al., *J. biol. Chem.*, 174, 265 (1948). 12) CHRISTIANSEN and JENSEN, *Acta chem. scand.*, 7, 1247 (1953); LAURENT and GERGELY, *J. biol. Chem.*, 212, 325 (1955). 13) HIRST and JONES, *Advanc. Carbohydr. Chem.*, 2, 235 (1946). 14) REEVES and GOEBEL, *J. biol. Chem.*, 139, 511 (1941).

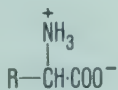
2. Amino Acids¹

An amino acid is any compound which contains one or more amino groups and one or more carboxylic acid groups. Those of biological importance generally contain an amino group in the α -position to a carboxyl group, i.e. they are of the general structure:



The asymmetry about the α -carbon atom renders the amino acids optically active, except when $\text{R} = \text{H}$, as in glycine. Their nomenclature is similar to that adopted for the carbohydrate series and involves the use of the small capital letters D and L to indicate their configuration about the α -carbon atom, sometimes followed by the sign of optical rotation in parentheses, e.g. L(+)-alanine. In the case of amino acids possessing two asymmetric centers, four stereoisomers are possible, and the isomer which has been found in proteins is referred to simply as the L-isomer. This is not, of course, a complete configurational description of this particular acid. (For the stereochemical configurations of amino acids see ².) The value of the specific rotation for any particular amino acid varies with concentration, temperature and hydrogen-ion concentration. A precise control of the experimental conditions is thus necessary for indicating the identity and purity of an acid by means of specific rotation values³.

The majority of amino acids are stable compounds and melt above 200°C with decomposition; they are insoluble in the common neutral solvents except water, and can usually be recrystallized from aqueous ethanol. Their salt-like behaviour can be ascribed to their existence as internal salts, or "zwitterions", i.e.



The amino acids behave as amphoteric compounds and possess characteristic isoelectric points; many of their physical properties exhibit maxima and minima at these points.

The separation and quantitative determination of amino acids have been revolutionized in recent years by the application of new procedures, such as adsorption chromatography on starch, partition chromatography on silica gel and paper, ion-exchange chromatography, and electrophoresis. A single ion-exchange column is now sufficient for the separation of all the common amino acids⁴. Many methods exist for the quantitative estimation of amino acids: isotope dilution, enzymatic assay, microbial assay and chemical methods^{1, 5}.

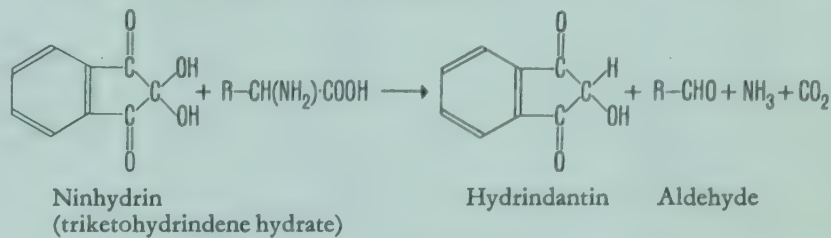
There are three methods of quantitative estimation which are applicable to the majority of amino acids:

- (a) Amino acids containing a primary amino group react with nitrous acid to give nitrogen:

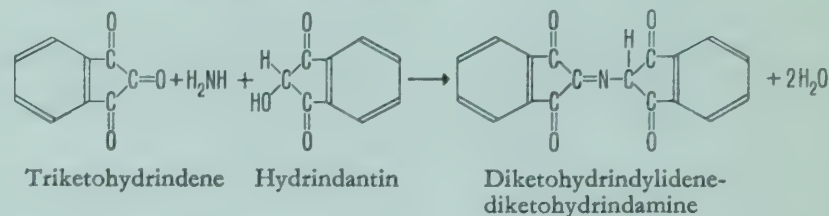


This forms the basis of VAN SLYKE's methods of estimation, the nitrogen being measured volumetrically⁶ or manometrically⁷.

- (b) Amino acids containing free carboxylic and primary α -amino groups are oxidized on heating with ninhydrin:



Either NH_3 or CO_2 can be quantitatively measured⁸. Alternatively, the blue color forming above pH 2 when the reaction mixture is heated, due to the following reaction, can be used for quantitative estimations⁹:



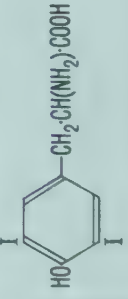


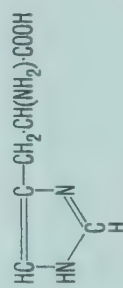
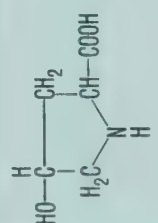
- (c) Formaldehyde reacts with the amino groups of an amino acid and thus reduces their basicity; this allows the acid to be directly titrated with alkali using phenolphthalein as indicator¹⁰.

The amino acids are the structural units of protein molecules and just over twenty have been established in this role (Table 7, pages 446–49). These are all α -amino acids of the L-configuration and there is no conclusive evidence that any other type of amino acid is a protein constituent². However, D-amino acids have been isolated from plants and microorganisms¹¹. The latter frequently elaborate polypeptides (often possessing antibiotic properties) containing D-amino acids; and indeed, the capsules of certain bacilli, e.g. *Bacillus anthracis*, consist almost wholly of polypeptides of D-glutamic acid. The amino acids listed in Table 8, pages 450–451 are not found in proteins but occur as intermediary metabolites or constituents of physiologically active compounds.

1) For reviews see GREENBERG, D. M. (Ed.), *Amino Acids and Proteins*, 1st ed., Springfield, Ill., 1951; NEURATH and BAILEY (Eds.), *The Proteins*, vol. IA, New York, 1953. 2) NEUBERGER, A., *Advanc. Protein Chem.*, **4**, 297 (1948). 3) For resolution of α -amino acids see GREENSTEIN, J. P., *Advanc. Protein Chem.*, **9**, 121 (1954). 4) MOORE and STEIN, *J. biol. Chem.*, **211**, 893 (1954). 5) Cf. TRISTRAM, G. R., in NEURATH and BAILEY (Eds.), *The Proteins*, vol. IA, New York, 1953; BLOCK and WEISS, *Amino Acid Handbook*, Springfield, Ill., 1956; BLOCK et al., *A Manual of Paper Chromatography and Paper Electrophoresis*, New York, 1955; BLOCK and BOLLING, *The Amino Acid Composition of Proteins and Foods*, 2nd ed., Springfield, Ill., 1951. 6) VAN SLYKE, D. D., *J. biol. Chem.*, **9**, 185 (1911); **12**, 275 (1912). 7) VAN SLYKE, D. D., *J. biol. Chem.*, **83**, 425 (1929). 8) VAN SLYKE et al., *J. biol. Chem.*, **141**, 627, 671 (1941); **150**, 251 (1943). 9) MOORE and STEIN, *J. biol. Chem.*, **176**, 367 (1948). 10) OL-COTT, H. S., in GREENBERG, D. M. (Ed.), *Amino Acids and Proteins*, 1st ed., Springfield, Ill., 1951, page 80. 11) THORNE, C. B., *Ann. Rev. Microbiol.*, **10**, 331 (1956).

Table 7 Physical and chemical properties of amino acids occurring as protein constituents

Name	Abbreviation*	Formula and mol.wt.	Structure	Elementary composition (%)			Solubility (grams per 100 g water at 25° C)	Specific rotation			Special properties Organism for microbiological assay	Special occurrence and biological function (for references see page 449)
				C	H	N		Temperature (°C)	Concentration**	Solvent		
α-Alanine (α-amino-propionic acid)	Ala.	C ₃ H ₇ NO ₂ 89.10	CH ₃ ·CH(NH ₂)·COOH	40.44	7.92	15.72	16.72	25 25 20	2.06 10.00 1.78	6-N HCl Water 3-N NaOH	<i>Leuconostoc (Lactobacillus) citrovorum</i> 8081	
Arginine (α-amino-δ-guanido- <i>n</i> -valeric acid)	Arg.	C ₆ H ₁₄ N ₄ O ₂ 174.21		41.37	8.10	32.16	15	23.3 20 20	1.65 3.48 0.87	6-N HCl Water 0.5-N NaOH	Basic. Gives SAKAGUCHI color reaction with α-naphthol and sodium hypochlorite <i>Streptococcus faecalis</i> 9790; <i>Leuconostoc citrovorum</i>	Intermediate in ornithine cycle of urea synthesis (see page 516) and in creatine synthesis (see page 511)
Asparagine (aspartic acid β-monoamide; α-amino-β-carbamyl-propionic acid)	Asp-NH ₂	C ₄ H ₈ N ₂ O ₃ 132.12	NH ₂ ·CO·CH ₂ ·CH(NH ₂)·COOH	36.37	6.11	21.21	2.46	20 20 20	2.24 1.41 11.23	3.4-N HCl Water 2.5-N NaOH	Hydrolyzed by hot acid or specific enzymes to give NH ₃ + aspartic acid	Found in free state in many plant tissues, especially etiolated seedlings
Aspartic acid (aminosuccinic acid)	Asp.	C ₄ H ₇ NO ₄ 133.11	HOOC·CH ₂ ·CH(NH ₂)·COOH	36.09	5.30	10.52	0.50	24 18 18	2.02 1.33 1.33	6-N HCl Water 3-N NaOH	Acidic. Yields 2 moles of CO ₂ and 1 mole of NH ₃ in ninhydrin reaction <i>Leuconostoc mesenteroides</i> P-60, 8042	Involved in transformation of citrulline to arginine (see page 516), and in biosynthesis of purines and pyrimidines (see pages 509 and 513)
Cysteine (α-amino-β-thiopropionic acid)	CySH	C ₃ H ₇ NO ₃ S 121.16	HS·CH ₂ ·CH(NH ₂)·COOH	29.73	5.82	11.56	very soluble	26	12.1	1-N HCl	Readily autoxidized in neutral or basic solution to cystine	Interconvertible with cystine by oxido-reduction (see page 480). Constituent of glutathione (see page 512). Some aromatic compounds are excreted in urine as derivatives of N-acetylcysteine (mercapturic acids) (see pages 516 and 519)
Cystine (di-[α-amino-propionic]-β-disulfide)	Cys.	C ₆ H ₁₂ N ₂ O ₄ S ₂ 240.31		29.99	5.03	11.66	0.011	24 18.5	1.0 0.4	1-N HCl 0.2-N NaOH	Readily reduced to cysteine <i>Leuconostoc mesenteroides</i> P-60, 8042; <i>Lactobacillus arabinosus</i>	Occurs abundantly in hair, keratin and insulin. The disulfide bond links together different polypeptide chains or different parts of the same polypeptide chain within the protein molecule
3,5-Diiodo-tyrosine***		C ₉ H ₉ NO ₃ I ₂ 433.00		24.97	2.10	3.23	0.062	20 20	5.08 4.41	1.1-N HCl 3.4-N NH ₄ OH		Occurrence confined to protein of thyroid gland (thyroid hormone*); see pages 181 and 514)

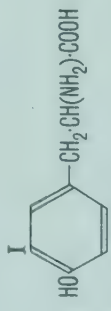

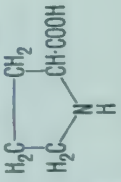
Glutamic acid (α-aminoglutaric acid)	Glu.	C ₆ H ₉ NO ₄ 147.14	HOOC-(CH ₂) ₂ -CH(NH ₂)-COOH	40.81	6.17	9.52	0.843	22.4 18 18	1.00 1.47 1.47	6-N HCl Water 1-N NaOH	+ 31.2 + 11.5 + 10.96	Acidic. On boiling in solution over a wide pH range (4-10) is cyclized to pyrrolidone-carboxylic acid <i>Leuconostoc mesenteroides</i> P-60, 8042; <i>Lactobacillus arabinosus</i>	Component of glutathione (see page 512) and of the folic acid vitamins (see page 219). Present in high concentration in tissues. More readily dehydrogenated in animal tissue than any other amino acid, and also more reactive in enzymic transamination reactions
Glutamine (glutamic acid β-monoamide; α-amino-γ-carbamyl-butyric acid)	Glu-NH ₂	C ₆ H ₁₀ N ₂ O ₃ 146.15	NH ₂ -CO-(CH ₂) ₂ -CH(NH ₂)-COOH	41.09	6.90	19.17	3.6 (at 18°C)	22	3.6	Water	+ 5.0	On heating in solution to ca. 100°C at near neutrality cyclizes to ammonium salt of pyrrolidonecarboxylic acid. Amide group reacts with nitrous acid in presence of acetic acid to release N ₂ . Hydrolyzed by specific enzyme to ammonium glutamate	Occurs in the free state in animal tissues and many plants, e.g. sugar beet. Phenylacetic acid is excreted by man as phenacetylglutamine (see pages 516 and 519)
Glycine (aminoacetic acid)	Gly.	C ₂ H ₅ NO ₂ 75.07	NH ₂ -CH ₂ -COOH	32.00	6.72	18.66	24.99					Optically inactive. Gives green color with o-phthalaldehyde <i>Leuconostoc mesenteroides</i> P-60, 8042	In many animals benzoic acid is excreted as benzoylglycine (hippuric acid) (see pages 516 and 519). Component of glutathione (see page 512). Metabolite in synthesis of creatine, porphyrins, purines, serine (see page 508)
Histidine (α-amino-β-[4-imidazole]-propionic acid)	His.	C ₆ H ₉ N ₃ O ₃ 155.16		46.44	5.85	27.09	4.29	25 25 20	1.00-4.05 0.75-3.77 0.77	6.1-N HCl Water 0.5-N NaOH	+ 13.34 - 38.95 - 10.9	Basic. Gives biuret test; couples with diazotized sulfonic acid to give intense red color (PAULY reaction) <i>Leuconostoc mesenteroides</i> P-60, 8042	Decarboxylated to histamine. Constituent of carnosine (β-alanylhistidine) found in muscle
δ-Hydroxylysine (α,ε-diamino-δ-hydroxy-n-caproic acid)		C ₆ H ₁₄ N ₂ O ₃ 162.19	NH ₂ -CH ₂ -CH(OH)-(CH ₂) ₂ -CH(NH ₂)-COOH	44.43	8.70	17.28		25	2.0	6-N HCl	+ 14.5	Reacts with periodate to yield formaldehyde and ammonia	Has been found as protein constituent only in collagen and gelatin. Phosphate ester occurs naturally ⁴
Hydroxyproline (γ-hydroxy-pyrrolidine-α-carboxylic acid)	Hypro.	C ₄ H ₆ NO ₃ 131.14		45.80	6.92	10.68	36.11	20 22.5 20	1.31 1.00 0.65	1-N HCl Water 0.5-N NaOH	- 47.3 - 75.2 - 70.6	Has no primary α-amino group and therefore differs in many respects from primary amino acids, e.g. with nitrous acid does not release nitrogen. Oxidized by hypochlorite to give hydroxyproline. Decarboxylated by ninhydrin to give reddish color below pH 4.4, yellowish color at higher pH. Forms bright blue condensation product with isatin	Present only in gelatin and collagen

* Used in the description of amino acid sequences in polypeptide and protein molecules.¹

** As grams per 100 ml solution, unless otherwise stated.

*** For chromatographic separation from other iodinated amino acids and estimation see ².

Table 7 Physical and chemical properties of amino acids occurring as protein constituents (continued)

Name	Abbreviation*	Formula and mol. wt.	Structure	Elementary composition (%)			Solubility (grams per 100 g water at 25°C)	Specific rotation			Special properties Organism for microbiological assay	Special occurrence and biological function (for references see page 449)
				C	H	N		Temperature (°C)	Concentration**	Solvent		
Leucine (α-amino- <i>isocaproic acid</i>)	Leu.	C ₆ H ₁₃ NO ₂ 131.18	<chem>(CH3)2CH-CH2-CH(NH2)-COOH</chem>	54.94	9.99	10.68	2.19	25	2.00	6-N HCl	<i>Lactobacillus arabinosus</i> 17-5, 8014; <i>Lactobacillus helveticus</i> ; <i>Streptococcus faecalis</i> ; <i>Leuconostoc mesenteroides</i> P-60, 8042	
<i>iso</i> Leucine (α-amino-β-methyl- <i>n</i> -valeric acid)	Ileu.	C ₆ H ₁₃ NO ₂ 131.18	<chem>CH3-CH2-CH2-CH(CH3)-CH(NH2)-COOH</chem>	54.94	9.99	10.68	2.93 (at 20°C)	20	5.09	6.1-N HCl	<i>Lactobacillus arabinosus</i> 17-5, 8014; <i>Lactobacillus helveticus</i> ; <i>Streptococcus faecalis</i> ; <i>Leuconostoc mesenteroides</i> P-60, 8042	
Lysine (α,ε-diamino- <i>n</i> -caproic acid)	Lys.	C ₆ H ₁₄ N ₂ O ₂ 146.19	<chem>NH2-(CH2)4-CH(NH2)-COOH</chem>	49.29	9.65	19.16	very soluble	23	2.00	6-N HCl	Basic. Can be precipitated with phosphotungstic acid. Dry heating of proteins containing lysine causes an apparent loss of lysine	
Methionine (α-amino-γ-methylthiol- <i>n</i> -butyric acid)	Mct.	C ₅ H ₁₁ NO ₂ S 149.22	<chem>CH3-S-CH2-CH2-CH(NH2)-COOH</chem>	40.24	7.43	9.39	3.35 (for DL-acid)	20	5.00	3-N HCl	<i>Leuconostoc mesenteroides</i> P-60, 8042; <i>Lactobacillus fermenti</i> 36 (for DL-acid)	Provides the sulfur atom for cysteine biosynthesis (see Cystathionine, Table 8, page 451). Carrier of "active" methyl groups
3-Monoiodo-tyrosine		C ₉ H ₉ NO ₃ I 307.10		35.15	3.27	4.557		20	5.0	1-N HCl		Occurrence confined to protein of thyroid gland (thyroid hormone ³ , see pages 181 and 514)
Norleucine (α-aminocaproic acid)		C ₆ H ₁₃ NO ₂ 131.18	<chem>CH3-(CH2)3-CH(NH2)-COOH</chem>	54.94	9.99	10.68	1.15 (at 18°C)	20	4.3	6-N HCl		Has not been proved to be a protein constituent ⁵
Phenylalanine (α-amino-β-phenylpropionic acid)	Phe.	C ₉ H ₉ NO ₂ 165.20		65.44	6.71	8.48	2.965	20	1.93	Water	<i>Leuconostoc mesenteroides</i> P-60, 8042	Can be converted to tyrosine in the human body (see page 481)
Proline (pyrrolidine-α-carboxylic acid)	Pro.	C ₅ H ₉ NO ₂ 115.14		52.16	7.88	12.17	162.3	20	0.57	0.5-N HCl	Neutral. Soluble in alcohol. Chemically very similar to hydroxyproline	
Serine (α-amino-β-hydroxypropionic acid)	Ser.	C ₃ H ₇ NO ₃ 105.10	<chem>HO-CH2-CH(NH2)-COOH</chem>	34.28	6.71	13.33	5.023 (for DL-acid)	25	9.34	1-N HCl	Split by periodate or lead tetraacetate to formaldehyde and glyoxylic acid. Gives biuret test. Acid hydrolysis of protein leads to partial destruction	Most of the serine in phosphoproteins (vitellin, casein) occurs in form of phosphoserine. ⁶ Phosphatidylserine is a component of some phospholipids

Threonine (β-methylserine; α-amino- β-hydroxy- butyric acid)	Thr.	C ₄ H ₉ NO ₃ 119.12		40.33	7.62	11.76		26	1.63 (g solute per 100 g solution)	Water	—	9.1	Some properties similar to those of serine. Oxidized by periodate to acetaldehyde and glyoxylic acid <i>Streptococcus faecalis</i> 9790; <i>Leu- conostoc mesenteroides</i> P-60, 8042	Phosphothreonine has been found in casein hydrolysates ⁷
Thyroxine (3,5,3',5'- tetraiodo- thyronine)		C ₁₅ H ₁₁ NO ₄ I ₄ 776.90		23.17	1.43	1.80	Iodine 65.35	0.001	3 (g solute per 100 g solution)	0.13-N NaOH in 70% ethanol	—	4.4		Occurrence confined to pro- tein of thyroid gland (thyroid hormone ⁸ ; see pages 181 and 514)
3,5,3'-Triiodo- thyronine		C ₁₅ H ₁₂ NO ₄ I ₃ 651.00		27.6	1.8	2.2	Iodine 58.5	29.5	4.75 (as hydro- chloride)	1-N HCl- ethanol (1:2)	+	21.5		Occurrence confined to pro- tein of thyroid gland (thyroid hormone ⁸ ; see pages 181 and 514)
Tryptophan (α-amino- β-[3-indolyl]- propionic acid)	Tyr.	C ₁₁ H ₁₂ N ₂ O ₂ 204.23		64.69	5.93	13.72	1.14	20 22.7 20	1.02 1.00 2.42	0.5-N HCl Water 0.5-N NaOH	+	2.4 31.5 6.17	Destroyed on prolonged heat- ing in hot acid. Gives MILLON reaction (see Tyrosine, below) and FOLIN test. Gives color reaction with p-dimethyl- aminobenzaldehyde and ni- trous acid (EHRlich test) <i>Lactobacillus arabinosus</i> 17-5, 8014; <i>Streptococcus faecalis</i>	
Tyrosine (α-amino-β-[p- hydroxyphenyl]- propionic acid)	Tyr.	C ₉ H ₉ NO ₃ 181.20		59.66	6.12	7.73	0.045	20 18	4.40 0.90	6.3-N HCl 3.0-N NaOH	—	8.64 13.2	Reacts with Hg salts and ni- trous acid to give red color (MILLON reaction). Other less specific color tests are: reac- tion with α-nitroso-β-naph- thol; reaction with FOLIN phenol reagent <i>Leuconostoc mesenteroides</i> P-60, 8042	Precursor of thyroxine ⁸ (see page 514), adrenalin (see page 513), melanin (see page 514)
Valine (α-amino- isovaleric acid)	Val.	C ₆ H ₁₁ NO ₂ 117.15		51.26	9.46	11.96	8.85	20 20	3.4 3.58	6-N HCl Water	+	28.8 6.42	<i>Lactobacillus arabinosus</i> 17-5, 8014; <i>Lactobacillus helveticus</i> ; <i>Streptococcus faecalis</i>	


* Used in the description of amino acid sequences in polypeptide and protein molecules.⁴
** As grams per 100 ml solution, unless otherwise stated.

References (Table 7)

1) BRAND and EDSELL, *Ann. Rev. Biochem.*, **16**, 223 (1947). 2) BLOCK and WEISS, *Amino Acid Handbook*, Springfield, Ill., 1956, page 37; ROCHE et al., in GLICK, D. (Ed.), *Methods of Biochemical Analysis*, vol. I, New York,

1954, page 243. 3) ROCHE and MICHEL, *Ann. Rev. Biochem.*, **23**, 481 (1954). 4) ASTRUP et al., *Acta physiol. scand.*, **24**, 202 (1952). 5) CONSDEN et al., *Biochem. J.*, **39**, 251 (1945). 6) ÅGREN et al., *Acta chem. scand.*, **5**, 324 (1951). 7) DE VERDIER, C.-H., *Nature*, **170**, 804 (1952).

Table 8 Physical and chemical properties of some amino acids not occurring in proteins but found in the free form

Name	Formula and mol.wt.	Structure	Elementary composition (%)			Solubility (grams per 100 g water at 25°C)	Specific rotation			Special properties	Occurrence and biological function (for references see page 451)
			C	H	N		Temperature (°C)	Concentration (g per 100 ml solution)	Solvent		
β-Alanine (β-amino-propionic acid)	C ₃ H ₇ NO ₂ 89.10	NH ₂ ·CH ₂ ·CH ₂ ·COOH	40.44	7.92	15.72	very soluble					Breakdown product of pyrimidines (see page 482). Occurs as constituent of pantothenic acid, coenzyme A, carnosine and anserine
α-Aminoadipic acid	C ₆ H ₁₁ NO ₄ 161.16	HOOC·(CH ₂) ₃ ·CH(NH ₂)·COOH	44.71	6.88	8.69	0.22 (at 20°C)				Decomposes on heating to α-piperidone-α'-carboxylic acid	Intermediate in breakdown of lysine (see page 480)
α-Amino- <i>n</i> -butyric acid	C ₄ H ₉ NO ₂ 103.12	CH ₃ ·CH ₂ ·CH(NH ₂)·COOH	46.60	8.80	13.59	28 (for DL-acid)	20	5.46	Water	+ 7.86	Found in brain preparations ¹ . Occurs as constituent of tripeptide ophthalmic acid in lens tissue ²
γ-Amino- <i>n</i> -butyric acid	C ₄ H ₉ NO ₂ 103.12	NH ₂ ·(CH ₂) ₃ ·COOH	46.60	8.80	13.59						Found in brain ³ , lung and heart ¹ preparations
β-Aminoisobutyric acid	C ₄ H ₉ NO ₂ 103.12	NH ₂ ·CH ₂ ·CH(CH ₃)·COOH	46.60	8.80	13.59						Breakdown product of thymine (see page 484)
δ-Aminolevulinic acid (γ-keto-δ-amino- <i>n</i> -valeric acid)	C ₅ H ₉ NO ₃ 131.14	NH ₂ ·CH ₂ ·CO·CH ₂ ·CH ₂ ·COOH	45.82	6.90	10.71					Reduces BENEDICT's solution in the cold. Split by periodate to formaldehyde and succinic acid	Intermediate in porphyrin biosynthesis (see page 511)
Carbamylaspartic acid (ureidosuccinic acid)	C ₅ H ₈ N ₂ O ₅ 176.14	HOOC·CH ₂ ·CH(COOH)·NH·CO·NH ₂	34.10	4.58	15.91	0.4 (at 20°C)	25		Water (Ba salt)	+ 24.1	Intermediate in biosynthesis of pyrimidines from aspartic acid in mammals and bacteria (see page 513)
Citrulline (α-amino-δ-ureido- <i>n</i> -valeric acid)	C ₆ H ₁₃ N ₃ O ₃ 175.19	NH ₂ ·CO·NH·(CH ₂) ₃ ·CH(NH ₂)·COOH	41.13	7.47	23.98		21.23 21.23	5.00 5.00	0.3-N HCl Water	+ 17.9 + 3.5	Intermediate in ornithine cycle of urea synthesis (see page 517)
Creatine (methyl-glycocyamine)	C ₄ H ₉ N ₃ O ₂ 131.14		36.64	6.92	32.05	1.35 (at 18°C)					Cell constituent. Creatine phosphate acts as store of "high energy" phosphate in vertebrate muscle (see page 511)

Creatinine (1-methylglyco- cyanidine)	$C_4H_7N_3O$ 113.12	$HN=C(N(CH_3) \cdot CH_2 \cdot CO$ 	42.48	6.24	37.15	8.7 (at 16°C)					Strongly basic	Present in urine
Cystathionine	$C_7H_{14}N_3O_4S$ 222.27	$HOOC \cdot CH(NH_2) \cdot CH_2 \cdot S \cdot CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot COOH$	37.82	6.35	12.60		22	1.0	1-N HCl	+ 23.7		Intermediate in transsulfuration of methionine with serine (see page 480)
Cysteic acid	$C_3H_7NO_4S$ 169.16	$HO_2S \cdot CH_2 \cdot CH(NH_2) \cdot COOH$	21.27	4.16	8.26		28	6.0	Water	+ 7.8		Intermediate in formation of taurine, a bile constituent, from cysteine
Ergothioneine (betaine of thiol- histidine)	$C_8H_{13}N_3O_4S$ 229.31		47.14	6.54	18.35		21	5.0	Water	+ 116.0	Basic. Stable to alkalis; thiol group is readily oxidized to sulfate under acid conditions. Gives reddish purple color with diazotized sulfanilic acid and alkali	Occurs in erythrocytes, liver, kidney, other tissues, and in urine and semen ⁴ . Constituent of ergot
Glycocyamine (guanidinoacetic acid)	$C_4H_7N_3O_3$ 117.11	$HN=C(NH_2) \cdot NH \cdot CH_2 \cdot COOH$	30.77	6.02	35.88	slightly soluble						In urine. Formed in kidney from arginine and glycine. Precursor of creatine and creatinine (see page 511)
Homoserine (α-amino- γ-hydroxy- n-butyric acid)	$C_4H_7NO_3$ 119.12	$HO \cdot CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot COOH$	40.33	7.62	11.76		24- 26	0.25	5-N HCl	+ 18.3		Intermediate in methionine metabolism (see page 479)
Ornithine (2,5-diamino- n-valeric acid)	$C_6H_{12}N_3O_3$ 132.17	$NH_2 \cdot (CH_2)_3 \cdot CH(NH_2) \cdot COOH$	45.42	9.15	21.19	very soluble	20	0.84	0.45-N HCl	+ 14.1	Formed from arginine by alkaline hydrolysis	Intermediate in ornithine cycle of urea synthesis (see page 516). Benzoic acid is excreted by the fowl as N,N'-dibenzoylornithine
Taurine (2-aminoethane- sulfonic acid)	$C_2H_7NO_3S$ 125.15	$NH_2 \cdot CH_2 \cdot CH_2 \cdot SO_3H$	19.19	5.64	11.19	8.78 (at 20°C)						In muscle tissue of invertebrates. Formed in mammalian liver from cysteine (see page 512). Component of taurocholic acid (bile acid)

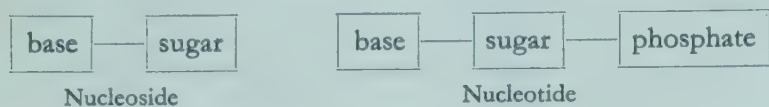
References (Table 8)

1) WALKER, D. M., *Biochem. J.*, **52**, 679 (1952). 2) WALEY, S. G., *Biochem. J.*, **64**, 715 (1956). 3) UDENFRIEND, S., *J. biol. Chem.*, **187**, 65 (1950). 4) For review of recent work see BELL, D. J., *Ann. Rep. Progr. Chem.*, **52**, 285 (1955).

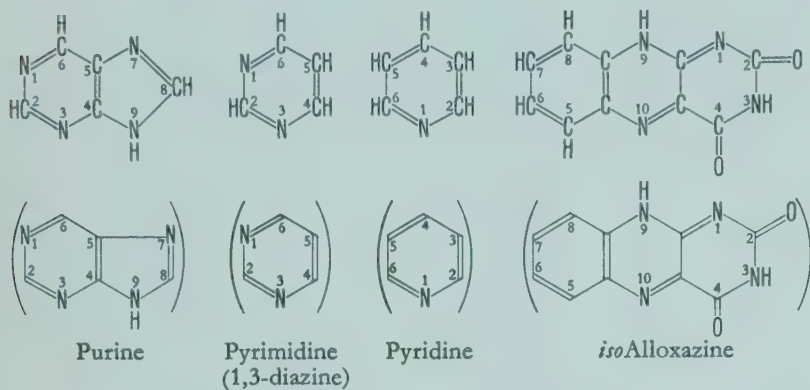
3. Nucleotides and related substances

Nucleosides and nucleotides

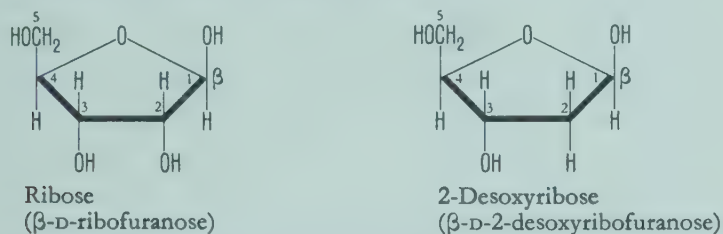
A *nucleoside* is a sugar linked to a heterocyclic base. A *nucleotide* is a nucleoside in which the sugar is esterified with phosphoric acid.



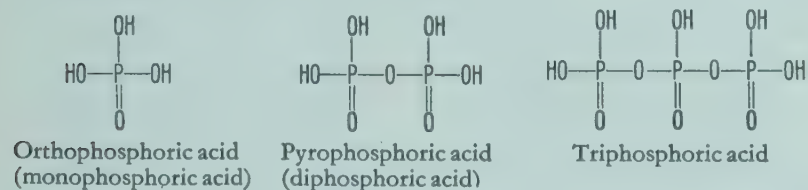
The bases found in nucleosides and nucleotides are most commonly purines and pyrimidines. Others include pyridines and *isalloxazines*. The parent compounds of these bases are:



The sugars found in nucleosides and nucleotides are most commonly either ribose or 2-desoxyribose:



The base-glycoside linkage of nucleosides and nucleotides occupies the 9-position in the case of purines and the 3-position in the case of pyrimidines. Esterification of nucleosides is not confined to orthophosphoric acid. It occurs also with pyrophosphoric (diphosphoric) acid and triphosphoric acid.

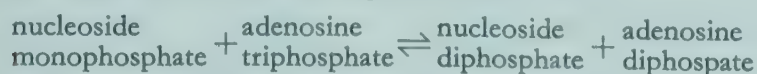


The nomenclature of the nucleosides and nucleotides is demonstrated by the examples given in Table 9 on page 453.

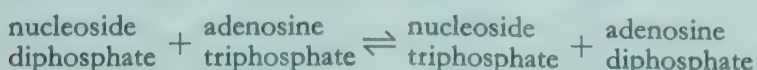
The naturally-occurring nucleoside mono-, di- and tri-phosphates have the sugar-phosphate ester linkage in the 5'-position. Exceptions are the nucleoside 3'-monophosphates and the nucleoside 3',5'-diphosphates formed during the enzymic digestion of ribonucleic acids (RNA). In the case of certain coenzymes, a nucleoside 2',5'-diphosphate or nucleoside 3',5'-diphosphate structure is also encountered (see Table 12, pages 460-466).

Nucleotides and polynucleotides (see under Nucleic acids, below) occur in all living cells. Certain naturally occurring bases, nucleosides and nucleotides have no known function apart from being intermediates in the synthesis or breakdown of other nucleotides (Tables 10 a, b, c, pages 454-458).

Nucleoside di- or tri-phosphates are precursors of the nucleic acids. They act also as carriers of the free energy of pyrophosphate bonds. In this capacity, nucleotides may be regarded as coenzymes of the free-energy transfer which occurs in many synthetic and degradative reactions. Nucleoside diphosphates are formed from the corresponding monophosphates by nucleoside monophosphate kinase. This enzyme is analogous in action to adenylate kinase and catalyzes the general reaction^{1, 2}:



Nucleoside triphosphates are formed in turn from the corresponding diphosphates by nucleoside diphosphate kinase^{1, 2}:



A list of nucleoside mono-, di- and tri-phosphates and their functions is given in Table 11, page 459.

The nucleotide coenzymes act as carriers of hydrogen (code-hydrogenases) and as carriers of the active forms of sugars, amino acids, fatty acids, dicarboxylic acids, carbon dioxide, and sulfate. The roles and modes of formation of nucleotide coenzymes are listed in Table 12, pages 460-466.

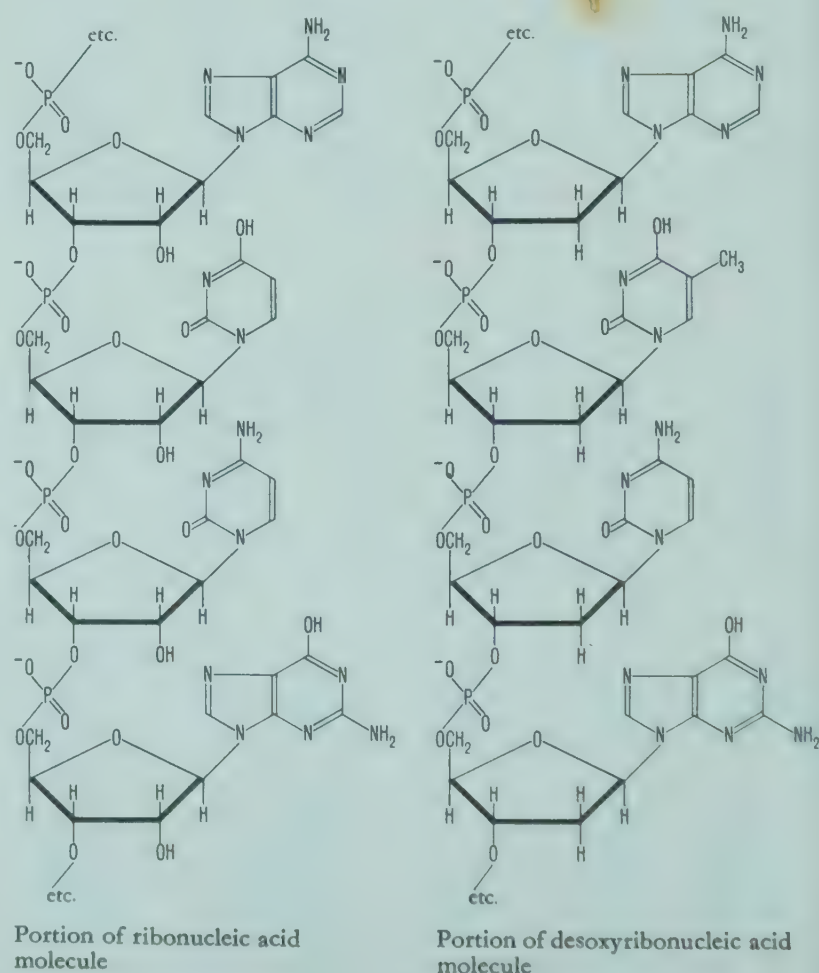
Nucleic Acids

Nucleic acid is the generic name given to a group of substances which, chemically speaking, are *polynucleotides*. Two types of nucleic acid are known: the *ribonucleic acids* (RNA) which are found in the cytoplasm and in small amounts in the nucleus of the cell; and the *desoxyribonucleic acids* (DNA) which are found in the nucleus of the cell. Both types of compound generally occur conjugated with proteins. The polynucleotide structure of RNA and DNA is formed by the esterification of the phosphate group of 5'-nucleotides with the 3'-position of adjacent nucleotides. Four nucleotide units are found in RNA. They are adenylic acid, guanylic acid, cytidylic acid and uridylic acid. Four desoxyribonucleotide units are found in most types of DNA. They are desoxyadenylic acid, desoxyguanylic acid, desoxycytidylic acid and desoxythymidylic acid. The latter desoxyribonucleotide is usually referred to simply as "thymidylic acid" because no naturally occurring ribonucleotide containing the base thymine has so far been found. In certain types of DNA one of these nucleotide units is replaced partially or wholly by a different one. These exceptions are indicated in Table 11, page 459. Portions of RNA and DNA polynucleotides are shown in Figure 4 below.

The sequences in which nucleotides occur in different types of nucleic acid are not known at present. The nucleotide composition of DNA is species-specific. Although the nucleotide composition of RNA differs between viruses, yeasts and animals, it has not yet been decided whether it is species-specific in animals. No significant quantitative differences in the nucleotide composition of RNA and DNA from different organs of the same animals have been detected, but the nucleotide composition of RNA isolated from the cytoplasm differs from that isolated from the nucleus. DNA contains equal amounts of desoxyguanylic acid and desoxycytidylic acid and also of desoxyadenylic acid and desoxythymidylic acid, the second pair being present in somewhat larger amounts in animals than in other organisms.

The DNA molecule consists of a pair of polynucleotide chains which are aligned in the form of a double helix. The alignment is such that bases in one chain are linked to bases in the other chain

Fig. 4 Portions of RNA and DNA polynucleotides



by hydrogen bonds, adenine being linked to thymine and guanine to cytosine. The structure of RNA is less well understood, but it may be analogous to that of DNA.

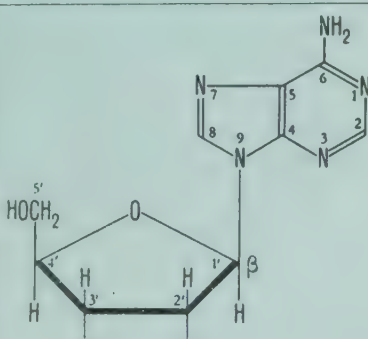
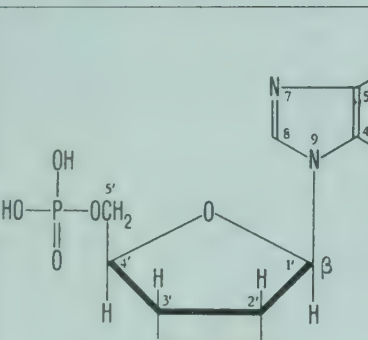
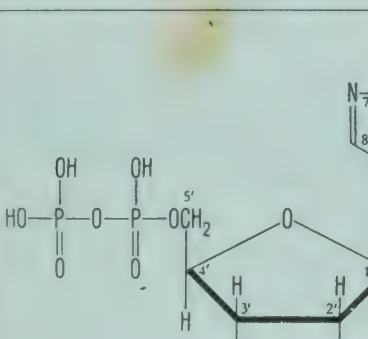
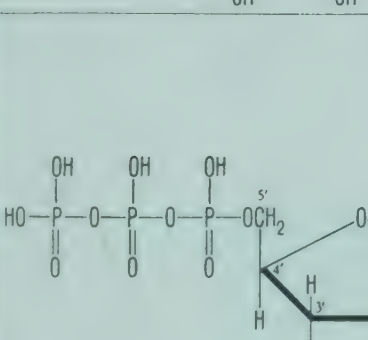
The molecular weights of the nucleic acids vary considerably with their method of preparation, artefacts of aggregation or disaggregation being possible. Molecular weights obtained for RNA correspond to chain lengths of between 30 and 1000 mononucleotide units. Values obtained for DNA correspond to chain lengths of between 1500 and 15,000 mononucleotide units.

The functions of nucleic acids are not fully understood. RNA plays an as yet ill-defined role in protein synthesis. DNA combined with protein (desoxyribonucleoprotein) makes up part or all of the constituent material of the chromosomes and genes³. According to current theory it forms both the “card index” of heredity and the “master templates” of cell reproduction. It has

been calculated that for a polynucleotide consisting of 300 mononucleotide units there can exist about 4×10^{87} different nucleic acids, assuming that there is complete freedom of choice in the arrangement of the four different mononucleotides⁴. The nucleic acids are thus capable of great specificity, and this specificity can be transferred to proteins during their synthesis in a manner as yet unknown⁵. The chemical basis of heredity is believed to lie in the sequences of nucleotides in the polynucleotide chain, different sequences of nucleotides reflecting specific types of information.

1) LIEBERMAN et al., *J. biol. Chem.*, **215**, 429 (1955). 2) GIBSON et al., *Biochim. biophys. Acta*, **21**, 86 (1956). 3) For a review see SINSHEIMER, R.L., *Science*, **125**, 1123 (1957). 4) DOUNCE, A. L., *Enzymologia (Amst.)*, **15**, 251 (1951–53). 5) GAMOW et al., *Advanc. biol. med. Phys.*, **4**, 23 (1956).

Table 9 Nomenclature of nucleosides and nucleotides

Structural formula	Group name*	Alternative group name*	Specific name**	Specific alternatives**
	Nucleoside	Riboside	Adenosine	Adenine riboside
	Nucleotide (Nucleoside mono-phosphate)	Ribotide (Riboside mono-phosphate)	5'-Adenylic acid (AMP)	Adenosine 5'-mono-phosphate Adenine nucleotide Adenine ribotide
	Nucleoside diphosphate	Riboside diphosphate	Adenosine diphosphate (ADP)	Adenosine 5'-pyrophosphate
	Nucleoside triphosphate	Riboside triphosphate	Adenosine triphosphate (ATP)	

* These are the names which can be applied to any compound of the above type. In general the terms nucleoside and nucleotide are reserved for derivatives of heterocyclic bases, whilst the terms riboside and ribotide are used for any type of base. The term nucleotide is expanded to ribonucleotide or desoxyribonucleotide when there is a possibility of confusion between these two types of compound. Alternatively, it is expanded to mononucleotide when it is necessary to distinguish between mononucleotides and polynucleotides. When necessary the position of the

phosphate ester linkage may be indicated. For example, the nucleotide shown is a 5'-nucleotide or, more fully, a 5'-ribonucleotide. The use of the bracketed group names is confined to occasions when it is necessary to distinguish between monophosphates and polyphosphates.

** When the nucleoside or nucleotide under consideration contains desoxyribose in place of ribose, this is made clear by prefixing the syllable desoxy to the name of the compound, for example, desoxyadenosine, desoxyadenylic acid.

Table 10 a Compounds involved in the biosynthesis and breakdown of purine and pyrimidine nucleotides: Purines and pyrimidines

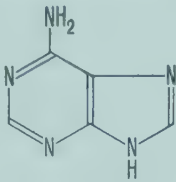
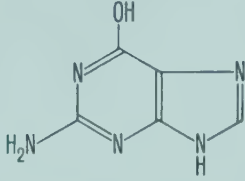
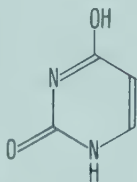
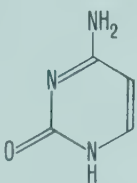
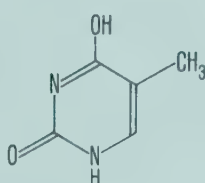
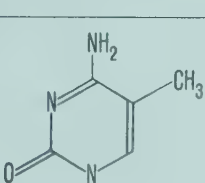
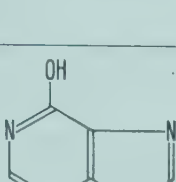
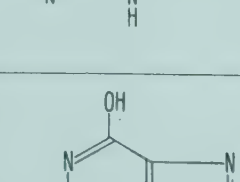
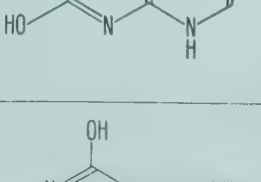
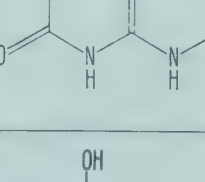
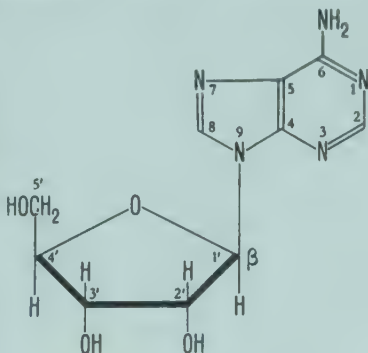
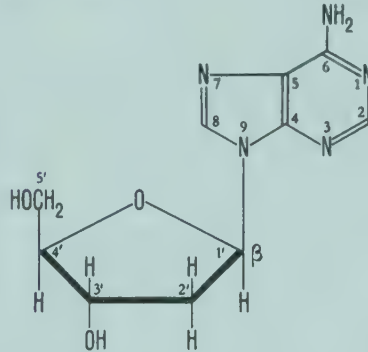
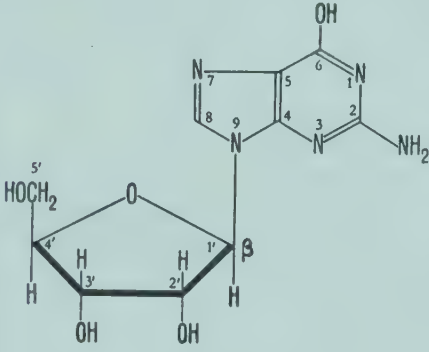
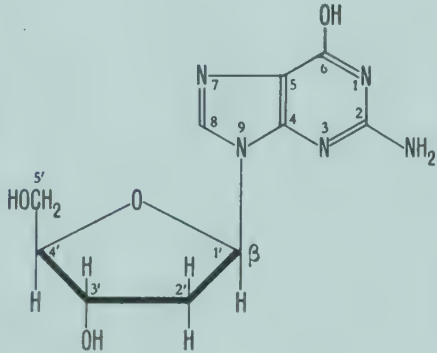
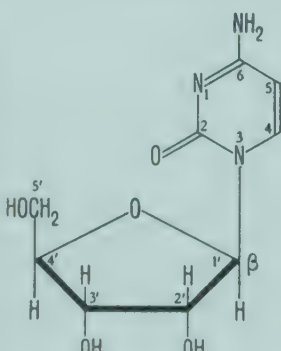
Name	Formula and mol.wt.	Structure	Properties	Occurrence	Function
Adenine (6-amino-purine)	$C_5H_5N_5$ 135.14		m.p. 365 °C (decomp.); picrate 298 °C	Occurs in tea, sugar beet, yeast, various animal or- gans	These bases are the products of the degradation of the corresponding nucleotides. They are further degraded by the pathways shown on pages 482–484. In mammals only adenine can be converted back to the corresponding nucleotide under normal conditions but the extent to which this occurs is uncertain
Guanine (2-amino-6-hydroxy-purine)	$C_5H_5ON_5$ 151.14		m.p. 365 °C (decomp.); picrate 258–260 °C	Occurs in scales and flesh of fish	
Uracil (2,6-dihydroxypyrimidine)	$C_4H_4O_2N_2$ 112.09		m.p. 338 °C (decomp.)		
Cytosine (6-amino-2-hydroxypyrimidine)	$C_4H_5ON_3$ 111.11		m.p. 320–325 °C (decomp.); picrate 333 °C		
Thymine (2,6-dihydroxy-5-methyl-pyrimidine)	$C_5H_6O_2N_2$ 126.12		m.p. 321–325 °C		
5-Methyl-cytosine (5-methyl-6-amino-2-hydroxypyrimidine)	$C_5H_7ON_3$ 125.14		m.p. 270 °C (decomp.); picrate 290–291 °C	Occurs in calf thymus nucleic acid and wheat germ DNA	
Hypoxanthine (6-hydroxypurine)	$C_5H_4ON_4$ 136.12		m.p. 150 °C (decomp.); picrate 246 °C	Occurs in muscle, meat extracts, blood, urine (the latter esp. in leukemia)	Product of deamination of adenine; precursor of xanthine
Xanthine (2,6-dihydroxypurine)	$C_5H_4O_2N_4$ 152.12		m.p. 262–264 °C (perchlorate)	Occurs in small quantities in plants, blood, liver, urine, yeast. Component of butterfly pigments and rare urinary calculi	Formed by oxidation of hypoxanthine, or by de- amination of guanine; precursor of uric acid
Uric acid (2,6,8-trihydroxypurine)	$C_5H_4O_3N_4$ 168.12		m.p. > 400 °C (decomp.) $d_{25}^{20} 1.836$	Occurs in urine and renal and urinary calculi (in- creased in urine and blood in gout, leukemia, ne- phritis, pneumonia). Also in feces of birds and rep- tiles	Formed by oxidation of xanthine. Chief product of nitrogen excretion in reptiles and birds. In mammals other than pri- mates further degraded to allantoin (see page 483)
Orotic acid (2,6-dihydroxypyrimidine-4-carboxylic acid)	$C_5H_4O_4N_2$ 156.10		m.p. 345–347 °C (decomp.); ethyl ester 200 °C	Occurs in milk	Precursor of orotidylic acid (see page 513)

Table 10 b Compounds involved in the biosynthesis and breakdown of purine and pyrimidine nucleotides: Nucleosides
The purine nucleosides listed in this table all contain 9-N-β-ribose or -deoxyribose linkages, the pyrimidine nucleosides 3-N-β-ribose or -deoxyribose linkages. For explanation of the nomenclature see Table 9, page 453

Name*	Formula and mol.wt.	Structure	Specific rotation	Function in mammalian tissue
Adenosine (adenine riboside)	C ₁₀ H ₁₃ O ₄ N ₅ 267.25		[α] _D ²⁰ – 67.3° (0.1-N NaOH)	<p>These nucleosides are products of the enzymic hydrolysis of the corresponding 3'- and 5'-nucleotides. The nucleosides in turn are broken down further by phosphorylation to yield ribose-1-phosphate or deoxyribose-1-phosphate and the corresponding base. Nucleoside kinases which form 5'-nucleotides from nucleosides plus ATP are known to occur in yeast and in some animal tissues. Their importance in mammals has not at present been assessed.</p>
Desoxyadenosine (adenine desoxyribose)	C ₁₀ H ₁₃ O ₃ N ₅ 251.25		[α] _D ²¹ – 26°	
Guanosine (guanine riboside)	C ₁₀ H ₁₃ O ₆ N ₅ 283.25		[α] _D ²⁰ – 60° (2% soln.)	
Desoxyguanosine (guanine desoxyribose)	C ₁₀ H ₁₃ O ₄ N ₅ 267.25		[α] _D ¹⁹ – 47.7° (1-N NaOH)	
Cytidine (cytosine riboside)	C ₉ H ₁₃ O ₅ N ₃ 243.23		[α] _D ²⁰ + 29.6°	

* The alternative name in "base riboside or desoxyribose" nomenclature is given in brackets.

Table 10 b Compounds involved in the biosynthesis and breakdown of purine and pyrimidine nucleotides: Nucleosides (continued)

Name*	Formula and mol.wt.	Structure	Specific rotation	Function in mammalian tissue
Desoxycytidine (cytosine desoxyriboside)	C ₉ H ₁₃ O ₄ N ₃ 227.23		[α] _D ²⁵ + 40°	
Uridine (uracil riboside)	C ₉ H ₁₂ O ₆ N ₂ 244.21		[α] _D ¹⁸ + 9.6°	These nucleosides are products of the enzymic hydrolysis of the corresponding 3'- and 5'-nucleotides. The nucleosides in turn are broken down further by phosphorolysis to yield ribose-1-phosphate or deoxyribose-1-phosphate and the corresponding base. Nucleoside kinases which form 5'-nucleotides from nucleosides plus ATP are known to occur in yeast and in some animal tissues. Their importance in mammals has not at present been assessed
(Desoxy)thymidine (thymine desoxyriboside)	C ₁₀ H ₁₄ O ₅ N ₂ 242.24		[α] _D ¹⁸ + 32.50° (1-N NaOH)	
Inosine (hypoxanthine riboside)	C ₁₀ H ₁₂ O ₅ N ₄ 268.24		[α] _D ¹⁸ – 72.45° (0.1-N NaOH)	

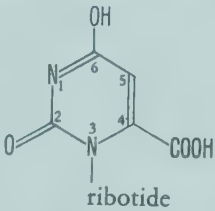
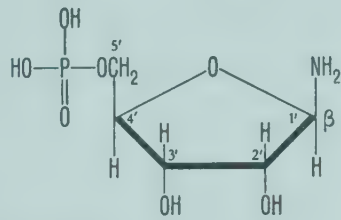
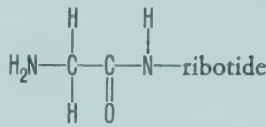
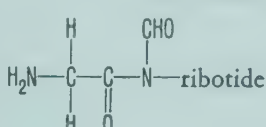
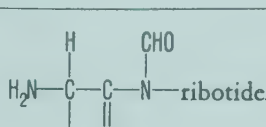
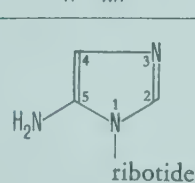
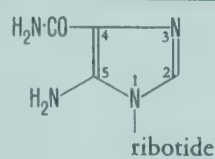
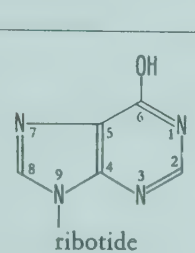
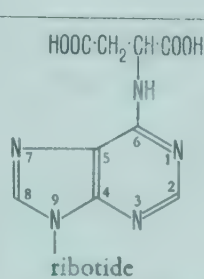
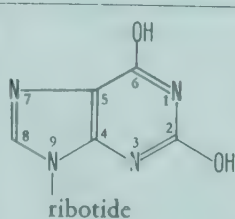
* The alternative name in “base riboside or desoxyriboside” nomenclature is given in brackets.

Table 10 b Compounds involved in the biosynthesis and breakdown of purine and pyrimidine nucleotides: Nucleosides (concluded)

Name*	Formula and mol.wt.	Structure	Specific rotation	Function in mammalian tissue
Desoxyinosine (hypoxanthine desoxyriboside)	$C_{10}H_{12}O_4N_4$ 252.24		$[\alpha]_D^{20} - 22.9^\circ$ (1-N NaOH)	These nucleosides have no known function other than their role as intermediates in the synthesis or breakdown of nucleotides (see page 483)
Xanthosine (xanthine riboside)	$C_{10}H_{12}O_6N_4$ 284.24		$[\alpha]_D^{30} - 51.21^\circ$	
Desoxyxanthosine (xanthine desoxyriboside)	$C_{10}H_{12}O_5N_4$ 268.24			
Uric acid riboside	$C_{10}H_{12}O_7N_4$ 300.24		$[\alpha]_D^{30} - 40.8^\circ$ (0.1-N NaOH)	

* The alternative name in “base riboside or desoxyriboside” nomenclature is given in brackets.

Table 10 c Compounds involved in the biosynthesis and breakdown of purine and pyrimidine nucleotides: Nucleotides
With the exception of inosinic acid, the compounds listed here have no known coenzyme activity

Name	Formula and mol.wt.	Structure*	Function
Orotidylic acid (OMP) (orotic acid ribotide)	C ₁₀ H ₁₃ O ₁₁ N ₂ P 368.21		Intermediate in biosynthesis of pyrimidine nucleotides. Formed from orotic acid (see page 513)
5-Phosphoribosylamine (p-ribosylamine 5-phosphate)	C ₅ H ₁₂ O ₇ NP 229.13		Intermediates in biosynthesis of inosinic acid (see pages 509–10)
Glycinamide ribotide	C ₇ H ₁₅ O ₈ N ₂ P 286.19		
Formylglycinamide ribotide	C ₈ H ₁₅ O ₉ N ₂ P 314.20		
Formylglycin-amidine ribotide	C ₈ H ₁₆ O ₈ N ₃ P 313.22		
5-Aminoimidazole ribotide	C ₈ H ₁₄ O ₇ N ₃ P 295.20		
5-Aminoimidazole-4-carboxamide ribotide	C ₉ H ₁₅ O ₈ N ₄ P 338.23		
Inosinic acid (IMP) (inosine 5'-phosphate)	C ₁₀ H ₁₃ O ₈ N ₄ P 348.22		Precursor of adenosine 5'-phosphate (AMP) and guanosine 5'-phosphate (GMP) (see Table 11). Can partially replace certain coenzyme functions of other nucleotides
Succinyladenylic acid (succinyladenosine 5'-phosphate)	C ₁₄ H ₁₈ O ₁₁ N ₅ P 463.31		Intermediate in synthesis of adenosine 5'-phosphate (AMP) from inosinic acid (see page 510)
Xanthidylic acid (XMP) (xanthosine 5'-phosphate)	C ₁₀ H ₁₃ O ₉ N ₄ P 364.22		Intermediate in synthesis of guanosine 5'-phosphate (GMP) from inosinic acid (see page 511)

* For structure of the “ribotide” portion of the molecule, see Table 9, page 453.

Table 11 Nucleoside mono-, di- and tri-phosphates (nucleotides)

Name	Abbreviation	Formula	Mol.wt.	Function
Adenosine 5'-monophosphate (adenylic acid)	AMP	$C_{10}H_{14}N_5O_7P$	347.24	Precursor of ADP. Activates phosphorylase b
Adenosine diphosphate	ADP	$C_{10}H_{15}N_5O_{10}P_2$	427.22	Immediate precursor of polynucleotides. For other functions see page 486
Adenosine triphosphate	ATP	$C_{10}H_{16}N_5O_{13}P_3$	507.20	Precursor of adenosine coenzymes (see Table 12, page 460). For other functions see page 486
Desoxyadenosine monophosphate	DAMP	$C_{10}H_{14}N_5O_6P$	331.24	Precursor of desoxyadenosine diphosphate
Desoxyadenosine diphosphate	DADP	$C_{10}H_{15}N_5O_9P_2$	411.22	Precursor of desoxyadenosine triphosphate
Desoxyadenosine triphosphate	DATP	$C_{10}H_{16}N_5O_{12}P_3$	491.20	Immediate precursor of desoxyribosepolynucleotides
Guanosine monophosphate (guanylic acid)	GMP	$C_{10}H_{14}N_6O_8P$	363.24	Precursor of guanosine diphosphate
Guanosine diphosphate	GDP	$C_{10}H_{15}N_6O_{11}P_2$	443.22	Immediate precursor of polynucleotides. Yields guanosine triphosphate during cleavage of succinyl-coenzyme A
Guanosine triphosphate	GTP	$C_{10}H_{16}N_6O_{14}P_3$	523.20	Precursor of guanosine coenzymes (see Table 12, page 463). Formed from orthophosphate and guanosine diphosphate during cleavage of succinyl-coenzyme A
Desoxyguanosine monophosphate (desoxyguanylic acid)	DGMP	$C_{10}H_{14}N_5O_7P$	347.24	Precursor of desoxyguanosine diphosphate
Desoxyguanosine diphosphate	DGDP	$C_{10}H_{15}N_5O_{10}P_2$	427.22	Precursor of desoxyguanosine triphosphate
Desoxyguanosine triphosphate	DGTP	$C_{10}H_{16}N_5O_{13}P_3$	507.20	Immediate precursor of desoxyribosepolynucleotides
Cytidine monophosphate (cytidylic acid)	CMP	$C_9H_{14}N_3O_8P$	323.21	Precursor of cytidine diphosphate
Cytidine diphosphate	CDP	$C_9H_{15}N_3O_{11}P_2$	403.19	Immediate precursor of polynucleotides. Precursor of cytidine triphosphate
Cytidine triphosphate	CTP	$C_9H_{16}N_3O_{14}P_3$	483.18	Precursor of cytidine coenzymes (see Table 12, pages 465–66)
Desoxycytidine monophosphate (desoxycytidylic acid)	DCMP	$C_9H_{14}N_3O_7P$	307.21	Precursor of desoxycytidine diphosphate
Desoxycytidine diphosphate	DCDP	$C_9H_{15}N_3O_{10}P_2$	387.19	Precursor of desoxycytidine triphosphate
Desoxycytidine triphosphate	DCTP	$C_9H_{16}N_3O_{13}P_3$	467.18	Immediate precursor of desoxyribosepolynucleotides
Uridine monophosphate* (uridylic acid)	UMP	$C_9H_{13}N_2O_8P$	324.19	Precursor of uridine diphosphate
Uridine diphosphate*	UDP	$C_9H_{14}N_2O_{11}P_2$	404.18	Immediate precursor of polynucleotides. Precursor of uridine triphosphate
Uridine triphosphate*	UTP	$C_9H_{15}N_2O_{14}P_3$	484.16	Precursor of uridine coenzymes (see Table 12, pages 463–65)
(Desoxy)thymidine monophosphate** (thymidylic acid)	(D)TMP	$C_{10}H_{15}N_2O_8P$	322.22	Precursor of desoxythymidine diphosphate
(Desoxy)thymidine diphosphate**	(D)TDP	$C_{10}H_{16}N_2O_{11}P_2$	402.20	Precursor of desoxythymidine triphosphate
(Desoxy)thymidine triphosphate**	(D)TTP	$C_{10}H_{17}N_2O_{14}P_3$	482.19	Immediate precursor of desoxyribosepolynucleotides
(Desoxy)-5-hydroxymethylcytidine monophosphate**	(D)HMCMP	$C_{10}H_{16}N_3O_8P$	337.24	Constituent nucleotide of the DNA of T ₂ , T ₄ and T ₆ bacteriophages of <i>Escherichia coli</i> , in which it replaces desoxycytidine monophosphate
(Desoxy)-5-methylcytidine monophosphate	(D)MCMP	$C_{10}H_{16}N_3O_7P$	321.24	Constituent of the DNA of wheat germ, in which it partially replaces desoxycytidine monophosphate

* The corresponding desoxyribose compounds are not known. ** The corresponding ribose compounds are not known.

Table 12 Nucleotides with coenzyme functions

Name	Formula and mol. wt.	Structure	Functions	Reference*
Nicotinamide mononucleotide (NMN)	$C_{11}H_{15}O_8N_2P$ 334.23		Constituent of di- and tri-phosphopyridine nucleotides (DPN and TPN)	1
Diphosphopyridine nucleotide (DPN) (adenosine diphosphate; nicotinamide riboside; codehydrogenase I; coenzyme I; α -DPN)	$C_{21}H_{27}O_{14}N_7P_3$ 663.45		Formed by the reaction: nicotinamide mononucleotide + ATP \rightarrow DPN + pyrophosphate. Coenzyme of many dehydrogenases, in which function the pyridine ring of the molecule is reduced reversibly as follows: 	1
Triphosphopyridine nucleotide (TPN) (2'-phospho-adenosine diphosphate; nicotinamide riboside; codehydrogenase II; coenzyme II)	$C_{31}H_{39}O_{17}N_7P_3$ 743.44		Formed by the reaction: DPN + ATP \rightarrow TPN + ADP. Coenzyme of many dehydrogenases, in which function the pyridine ring of the molecule is reduced reversibly as shown above	1

* For references see page 466.

Table 12 Nucleotides with coenzyme functions (continued)

Name	Formula and mol. wt.	Structure	Functions	Reference*
Flavin mononucleotide (FMN) (flavin ribityl phosphate)	$C_{17}H_{21}O_6N_4P$ 456.36		Constituent of flavin adenine dinucleotide (see below)	2
Flavin adenine dinucleotide (FAD) (adenosine diphosphoflavin ribitol)	$C_{27}H_{33}O_{10}N_7P_2$ 785.58		Formed by the reaction: flavin mononucleotide + ATP → flavin adenine dinucleotide + pyrophosphate. Prosthetic group of flavin enzymes (e.g. DPN- and TPN-cytochrome reductases, D-amino acid oxidase, succinic dehydrogenase, xanthine oxidase)	2
Coenzyme A (CoA)	$C_{21}H_{38}O_{10}N_4P_3S$ 767.57		Coenzyme of acyl-group transfer. Formed from pantothenic acid, cysteine and ATP. Acyl groups combine with the sulfhydryl group of CoA to form thiol esters, e.g. AMP + CO · CH ₃ + R · SH → AMP + R · S · CO · CH ₃ CoA is involved in the following reactions: formation of citrate from oxaloacetate and acetate (page 473), oxidation of pyruvate (page 474), oxidation of α-ketoglutarate (page 473), oxidation and synthesis of fatty acids (page 474), synthesis of neutral fat (page 503) and phospholipids (page 502), and in the acetylation of amines (page 518), choline (page 508) and glucosamine	3

Acyl adenosine monophosphates	—	<p>where $R = CH_3 \cdot (CH_2)_n^-$</p>	4	Formed by the reaction: fatty acid + ATP → acyl adenosine monophosphate + pyrophosphate. Intermediate in activation of acetic acid and other fatty acids (page 474)
Aminoacyl adenosine monophosphates	—	<p>where $R = \text{amino-acid residue}$</p>	5	Intermediate in activation of amino acids for protein synthesis
Adenosine diphosphate aspartic acid	$C_{14}H_{30}O_{11}N_6P_2$ 510.31		6	Function unknown. Possibly intermediate in formation of asparagine. The β-carboxyl linkage is not established with certainty
Adenosine diphosphate glutamic acid	$C_{15}H_{32}O_{13}N_6P_2$ 556.34		6	Function unknown. Possibly intermediate in formation of glutamine and γ-glutamyl peptides. The γ-carboxyl linkage is not established with certainty

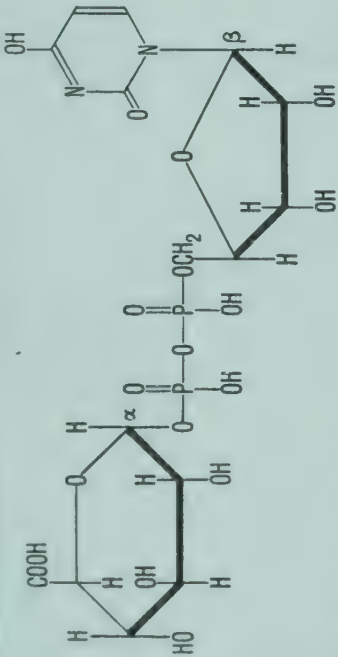
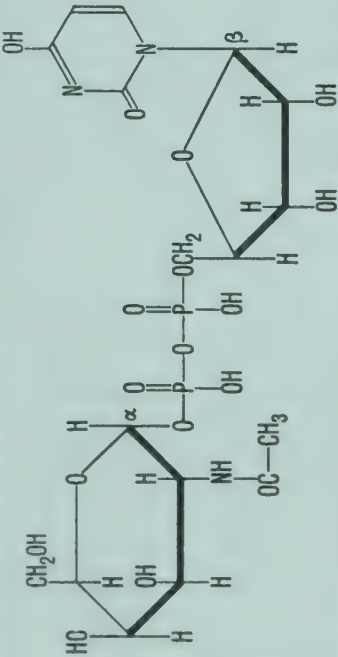
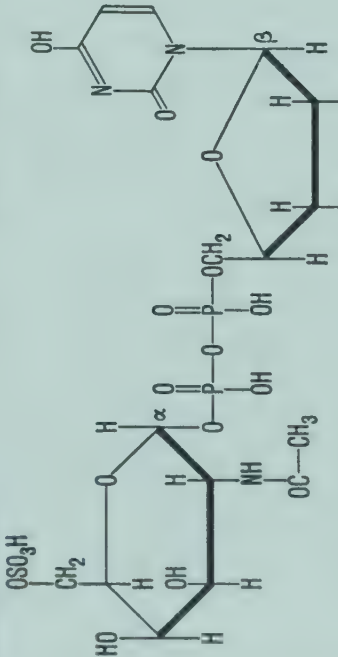
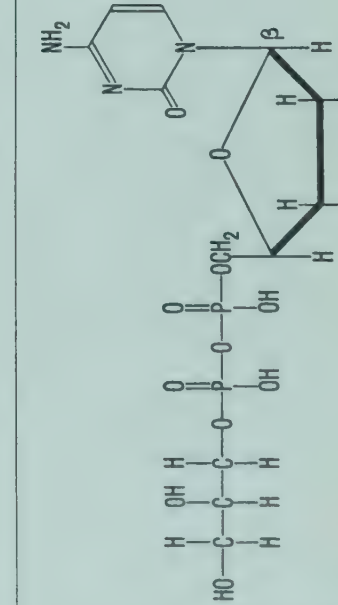
* For references see page 466.

Table 12 Nucleotides with coenzyme functions (continued)

Name	Formula and mol. wt.	Structure	Functions	Reference*
Adenosine 5'-phosphosulfate	$C_{10}H_{14}O_{10}N_6P_2S$ 427.30		Formed from ATP and inorganic sulfate. Intermediate in sulfate ester synthesis (see page 519)	7
Adenosine 3'-phosphate 5'-phosphosulfate	$C_{10}H_{15}O_{13}N_6P_3S$ 507.29		Formed from adenosine 5'-phosphosulfate and ATP. Donor of sulfate group in formation of esters of sulfuric acid (see page 519)	7
Guanosine diphosphate mannose	$C_{18}H_{26}O_{15}N_5P_3$ 604.38		Probably intermediate in interconversions involving mannose. Formed from mannose-1-phosphate and guanosine triphosphate	8
Uridine diphosphate glucose	$C_{15}H_{24}O_{17}N_2P_2$ 566.32		Formed by the reaction: glucose-1-phosphate + UTP → uridine diphosphate glucose + pyrophosphate. Precursor of uridine diphosphate glucuronic acid (see below). Intermediate in interconversion of glucose and galactose: uridine diphosphate glucose \xrightleftharpoons{DPN} uridine diphosphate galactose. In this reaction DPN is required for the consecutive oxidation and reduction of the 4-position of the hexose ring: $H-C(=O)-CH_2-CH(OH)-CH(OH)-CH_2-OH + DPN \rightleftharpoons H-C(=O)-CH_2-CH(OH)-CH(OH)-C(=O)-H + DPNH_2 + DPN$	9

Uridine diphosphate galactose	$C_{15}H_{24}O_{17}N_3P_3$ 566.32		Intermediate in interconversion of galactose and glucose (see above). Probably intermediate in formation of lactose	9
Uridine diphosphate glucosamine	$C_{15}H_{25}O_{16}N_3P_3$ 565.34		Intermediate in synthesis of mucopolysaccharides. Formed from uridine triphosphate and glucosamine-1-phosphate	10
Uridine diphosphate N-acetyl- glucosamine	$C_{17}H_{27}O_{17}N_3P_3$ 607.38		Intermediate in synthesis of mucopolysaccharides and glyco- proteins	11
Uridine diphosphate acetylglucosamine phosphate	$C_{17}H_{28}O_{20}N_3P_3$ 687.36		Intermediate in synthesis of mucopolysaccharides and glycoproteins	12

Table 12 Nucleotides with coenzyme functions (concluded)

Name	Formula and mol. wt.	Structure	Functions	Reference*
Uridine diphosphate glucuronic acid	$C_{18}H_{23}O_{18}N_3P_3$ 580.31		Formed from uridine diphosphate glucose by DPN-dependent oxidation. Donor of glucuronic acid in formation of glucuronoside detoxication products, and probably also in formation of polysaccharides containing glucuronic acid (see also page 502)	13
Uridine diphosphate N-acetyl-galactosamine	$C_{17}H_{27}O_{17}N_3P_3$ 607.38		Probably intermediate in synthesis of mucopolysaccharides	14
Uridine diphosphate N-acetyl-galactosamine sulfate	$C_{17}H_{27}O_{18}N_3P_3S$ 687.44		Intermediate in synthesis of mucopolysaccharides	15
Cytidine diphosphate glycerol	$C_{11}H_{21}O_{13}N_3P_3$ 477.27		Function unknown	16

Cytidine diphosphate ribose	$C_{14}H_{26}O_{16}N_3P_2$ 537.33		Function unknown	16
Cytidine diphosphate choline	$C_{14}H_{26}O_{11}N_4P_2$ 488.34		Formed from cytidine triphosphate and phosphorylcholine. Involved in formation of lecithin: cytidine diphosphate choline + α,β -diglyceride \rightarrow lecithin + cytidine monophosphate (see also page 502)	17
Cytidine diphosphate ethanolamine	$C_{11}H_{20}O_{11}N_4P_2$ 446.26		Formed from cytidine triphosphate and phosphorylethanolamine. Involved in formation of cephalin (phosphatidylethanolamine) (see also page 502)	17

References (Table 12)

1) RACKER, E., *Physiol. Rev.*, **35**, 1 (1955). 2) WHITE et al., *Principles of Biochemistry*, London, 1954. 3) LIPMANN, F., *Bact. Rev.*, **17**, 1 (1953); WARD et al., *J. biol. Chem.*, **213**, 869 (1955); HOAGLAND and NOVELLI, *J. biol. Chem.*, **207**, 767 (1954). 4) BERG, P., *J. biol. Chem.*, **222**, 991, 1015 (1956). 5) HOAGLAND et al., *J. biol. Chem.*, **218**, 345 (1956); KELLER and ZAMECNIK, *J. biol. Chem.*, **224**, 45 (1956); BERG, P., *J. biol. Chem.*, **222**, 1025 (1956). 6) HANSEN and HAGEMAN, *Arch. Biochem. Biophys.*, **62**, 511 (1956). 7) ROBBINS and LIPMANN, *J. Amer. chem. Soc.*, **78**, 2652, 6409 (1956); BANDURSKI et al., *J. Amer. chem. Soc.*, **78**, 6408 (1956). 8) CABIB and LELOIR, *J. biol. Chem.*, **206**, 779 (1953); STROMINGER, J. L., *Fed. Proc.*, **13**, 307 (1954); MUNCH-PETERSEN, A., *Arch. Biochem. Biophys.*, **55**, 592 (1955). 9) CAPUTO et al., *J. biol. Chem.*, **184**, 333 (1950); MAXWELL, E. S., *J. Amer. chem. Soc.*, **78**, 1074 (1956); PARK, J. T., *J. biol. Chem.*, **194**, 885 (1952); GANDER et al., *Arch. Biochem. Biophys.*, **60**, 259 (1956). 10) MALEY et al., *J. Amer. chem. Soc.*, **78**, 5303 (1956). 11) CABIB et al., *J. biol. Chem.*, **203**, 1055 (1953). 12) STROMINGER, J. L., *Biochim. biophys. Acta*, **17**, 283 (1955). 13) STOREY and DUTTON, *Biochem. J.*, **59**, 279 (1955); SMITH and MILLS, *Biochim. biophys. Acta*, **13**, 386 (1954); STROMINGER et al., *J. biol. Chem.*, **224**, 79 (1957). 14) PONTIS, H. G., *J. biol. Chem.*, **216**, 195 (1955). 15) STROMINGER, J. L., *Biochim. biophys. Acta*, **17**, 283 (1955). 16) BADDILEY et al., *J. chem. Soc. Lond.*, **1956**, 4186, 4583; *Biochem. J.*, **63**, 15P (1956). 17) KENNEDY, E. P., *J. biol. Chem.*, **222**, 185 (1956); KENNEDY and WEISS, *J. biol. Chem.*, **222**, 193 (1956).

4. Enzymes

Enzymes are protein catalysts which range in molecular weight from about 13,000 (lysozyme, ribonuclease) up to as much as 840,000 (myosin). They are purified and isolated by the use of techniques for fractionating proteins¹. Their general properties will be described in the section which follows. The specific enzymes responsible for digestion are dealt with on pages 487–498.

Nomenclature of enzymes

Enzymes are usually given names which indicate both the principal substrate and the reaction catalyzed (e.g. malic dehydrogenase). Many enzymes have, however, been given trivial names and these are often a cause of confusion.

The word “enzyme” usually denotes a catalytic protein plus any component that cannot be readily removed from the protein without denaturing it. The usage is not, however, very rigid for in some contexts “enzyme” is intended to include dissociable cofactors and in others to indicate the catalytic protein *per se*. If there is danger of ambiguity, the catalytic protein is denoted by the term “*apo-enzyme*” and the protein plus cofactors by “*holo-enzyme*”.

Coenzymes or *prosthetic groups* are nonprotein organic compounds which, in combination with the apo-enzyme, play an intimate part in the catalysis by the enzyme. There is no generally-accepted distinction between coenzymes and prosthetic groups, but the latter name is usually reserved for groups that are bound relatively firmly by the protein. “*Activators*” are usually distinguished from coenzymes in being small ions that are required by some enzymes for full catalytic activity. Some enzymes do not appear to possess a prosthetic group or coenzyme nor do they require an activator.

Specificity of enzymes²

Although nearly all the individual reactions of intermediary metabolism are catalyzed by separate enzymes (see pages 472–486), few of these enzymes are absolutely specific to the structure of their substrates. Most enzymes can act on close structural analogues of their physiological substrates, although usually at much reduced rates, whilst a few enzymes can act on a relatively wide group of substrates. Like any other catalyst, an enzyme acts in both the forward and reverse reactions, but the extent of the reversibility is determined by the equilibrium of the reaction being catalyzed and the availability of the necessary reactants.

There are no completely general rules of enzyme specificity, for in different enzyme systems different parts of the substrate molecule appear to be important. Thus, the lipases require an ester bond in their substrates but there can be very considerable variation in the structures of the groups adjoining this susceptible bond. On the other hand, chymotrypsin and trypsin require certain configurations in the neighborhood of the susceptible bond, but the nature of the bond itself can vary. For example, these enzymes will hydrolyze peptide bonds in protein substrates but in certain artificial substrates (e.g. methyl cinnamate) ester bonds can be hydrolyzed.

An added complication is that those hydrolytic enzymes which can act on several substrates are usually capable of catalyzing a transferring reaction in which an alcohol or an amine replaces the water. Many of these transfer reactions are unlikely to be of physiological significance because of the prevalence of water molecules under physiological conditions.

Many enzymes show stereochemical specificity in being unable to attack geometrical or optical isomers of their substrates. Less specific enzymes such as the esterases can, however, attack stereochemical isomers although usually at reduced rates.

Mechanism of enzyme action

Enzymes combine with their substrates at three or more points³. An attractive hypothesis is that after the formation of this enzyme-substrate compound there is a simultaneous attack on the substrate by two groups of the enzyme, one withdrawing an electron and the other donating an electron to a different atom of the substrate and thus promoting the reaction of the substrate⁴. Such a bifunctional attack would be analogous to the catalytic hydrolysis of glycosides by 2-hydroxypyridine⁵ and would explain why enzymes are much more effective catalysts than monofunctional catalysts such as acids or bases.

Some enzymes have been found to retain their activity after much selective chemical modification or enzymic degradation⁶. Only part of the enzyme protein is therefore essential for catalytic activity.

Equilibrium. Although an enzyme may induce a reaction that cannot be appreciably detected in its absence, the enzyme cannot affect the equilibrium position.

Enzyme kinetics⁷

When an enzyme is added to a suitable reaction mixture, there is first a very short lag before a steady rate of reaction is attained⁸. This lag is so short that it is not detectable when the rate is obtained from measurements made at intervals of one minute or longer. Once established, the rate remains constant for a period which may sometimes be as long as several hours, although in other cases it may be only a few minutes. The rate of reaction begins to fall after this period because of reduced substrate concentration and/or the accumulation of products. This decrease in reaction rate is not easily analyzed mathematically and it is therefore usual to study only the constant reaction rate. The following discussion is confined to this constant reaction rate.

If the enzyme is susceptible to inhibition by excess substrate (see below) the rate may at first increase as the inhibition is relieved by removal of the substrate.

Enzyme concentration. The reaction rate is usually proportional to the concentration of enzyme. Strict linearity may not always be achieved experimentally, for instance because the enzyme preparation may contain a dissociable activator or inhibitor or the enzyme may be unstable at low concentrations. Alternatively, the reaction may have proceeded so far that the rate has already commenced to fall off at the highest enzyme concentrations.

Hydrogen-ion concentration. Most enzymes possess well-defined pH optima with appreciable activity over a range of only 2–3 pH units. Some enzymes are inhibited by some of the buffers in common use. It is therefore often worthwhile to compare the results in one buffer with those obtained in another type of buffer solution of the same pH range.

The study of kinetic data obtained at different pH values with different substrates and different concentrations of a single substrate is of use in investigating the details of enzyme mechanisms^{9, 10}. For other purposes, the variations in the pH curve with different substrates and substrate concentrations are not usually important.

Temperature. The rate of an enzyme-catalyzed reaction increases by a factor which is usually 1.5–3 for every rise of 10 °C. There is, however, an optimum temperature above which further increase reduces the amount of substrate reacting because the enzyme becomes inactivated. The optimum temperature for short-term experiments (e.g. of one hour duration) is often about 50 °C. Most mammalian enzymes show little inactivation in the presence of their cofactors and substrates at 37 °C so that this is usually a suitable temperature to study the reaction. It is not desirable to increase the temperature to the optimum because the rate of enzyme inactivation, and therefore the optimum temperature, is often greatly influenced by slight changes of the experimental conditions.

Substrate concentration. As the initial substrate concentration is increased, the rate of reaction is at first proportional to this concentration, but at higher values it usually becomes virtually independent of it. This relation can be justified theoretically by considering a mechanism such as

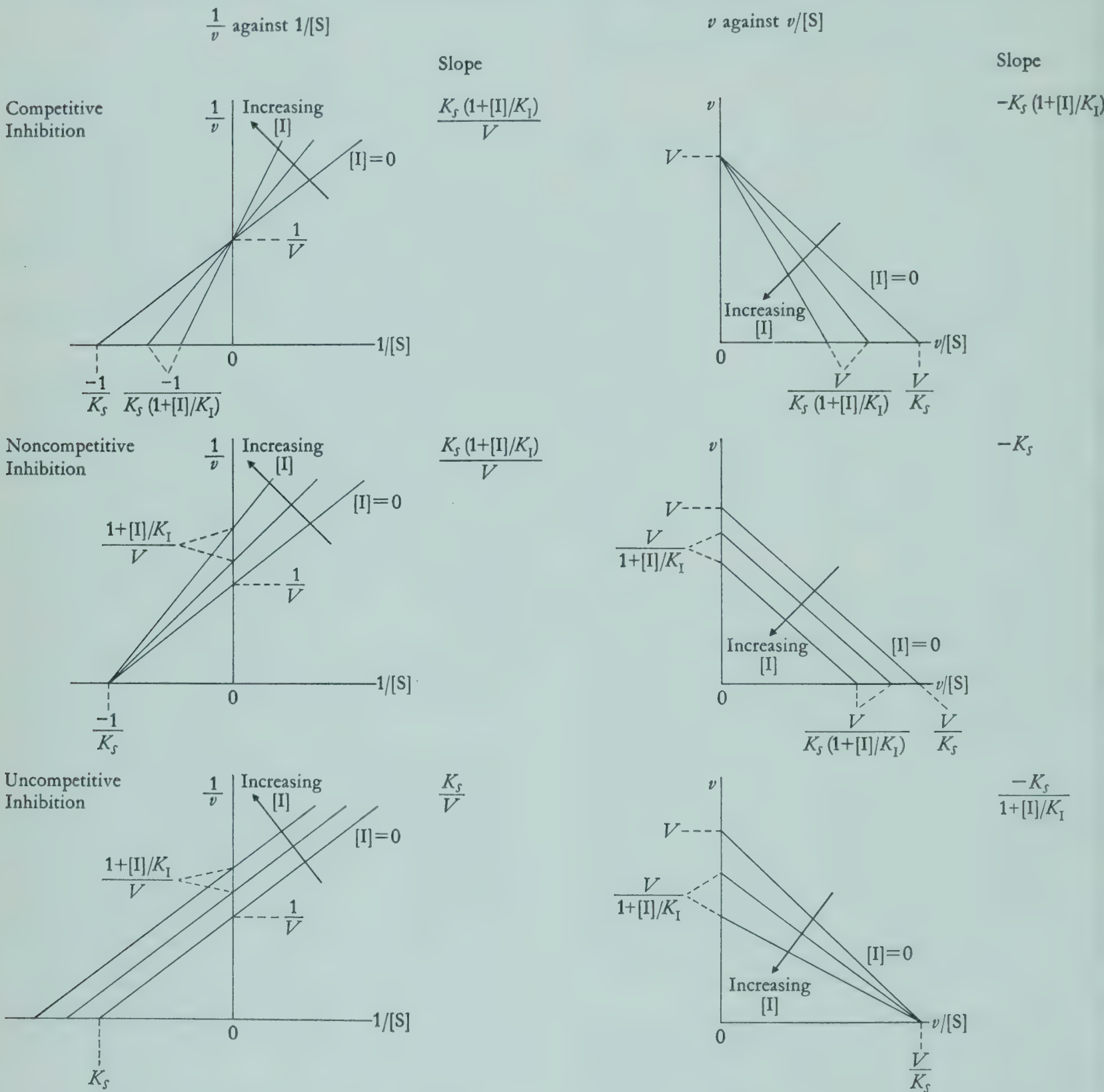


where E is the enzyme, S the substrate, ES the enzyme-substrate compound, P the products, and k_1 , k_2 and k_3 the rate constants of the three reactions. The constant steady-state velocity v is given by

$$(2) \quad v = \frac{V[S]}{K_s + [S]}$$

where V is the maximum velocity obtained at high substrate concentrations, $[S]$ the concentration of substrate, and K_s a quantity which is termed the “MICHAELIS constant”. $[S]$ is strictly the concentration of substrate not combined with the enzyme but the amount of enzyme is usually so low that there is virtually no difference between the concentrations of free and total substrate. Mathematically, V is given by k_3e where e is the total concentration of enzyme present. K_s is given by $(k_2 + k_3)/k_1$ and has the dimensions of concentration. Although K_s is independent of both $[S]$ and e , it usually changes with pH, temperature, different substrates and the cofactor concentration. K_s may sometimes change with ionic strength or with different buffers and, like other characteristics of enzymes, it may differ for similar enzymes from different sources.

Fig. 5 Inhibition data plotted according to Table 13
Each line represents data for a series of substrate concentrations. One line of each graph is without inhibition and the other two are for two different concentrations of inhibitor



Equation (2) was first obtained theoretically by MICHAELIS and MENTEN¹² who assumed that the second reaction of mechanism (1) was the rate-limiting step. Under these conditions k_2 is much greater than k_3 , and K_s becomes k_3/k_1 , which is the dissociation constant of the enzyme-substrate compound. This assumption is known to be valid for some enzymes but not for others⁴.

Evaluation of MICHAELIS constant K_s and maximum velocity V . K_s may be evaluated as being equal to the concentration of substrate at which the velocity is half the maximum. This may be done by plotting the curve of v against $[S]$. The experimental data can, however, be used more efficiently by plotting certain functions of v and $[S]$ as shown in Table 13¹². These plots give straight lines if equation (2) is obeyed. The plot of $1/v$ against $1/[S]$ has the advantage that the variables are separate and the calculations for plotting are thus quicker. Unfortunately the points are not evenly spread and the errors at low values of v are accentuated. This method gives accurate values for V but less accurate estimates for K_s . The second method (Table 13) is usually the most satisfactory for evaluating both K_s and V .

It is sometimes convenient, such as when comparing different substrates, to plot v against $\log [S]$. This plot gives an S-shaped

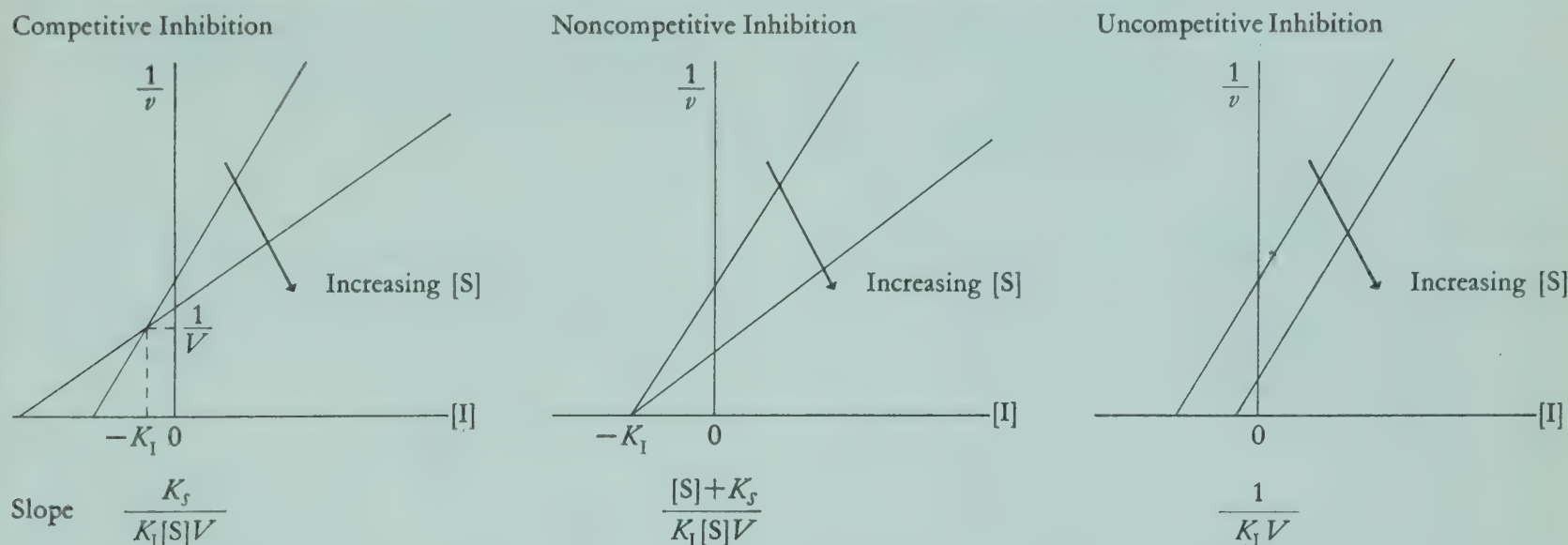
Table 13 Linear plots for evaluating MICHAELIS constant K_s and maximum velocity V
The plot of v against $v/[S]$ is usually the most satisfactory

Plot		Slope	Intercept	
Ordinate	Abcissa		Ordinate	Abcissa
$1/v$	$1/[S]$	K_s/V	$1/V$	$-1/K_s$
v	$v/[S]$	$-K_s$	V	V/K_s
$[S]/v$	$[S]$	$1/V$	K_s/V	$-K_s$

curve instead of a straight line; the inflection of this curve occurs at a value of $\log [S]$ equal to $\log K_s$.

Inhibition by excess substrate. This phenomenon occurs with some enzymes and is usually explained by postulating that the enzyme-substrate compound (ES) combines with a second molecule of S to form an inactive complex which unless it reverts to the origi-

Fig. 6 Inhibition data: Plots of $1/v$ against $[I]$ ¹⁶

 Each line represents data for a series of inhibitor concentrations $[I]$ but at different substrate concentrations $[S]$


nal ES form, can yield products only slowly or not at all. When v is plotted against $\log [S]$, this mechanism predicts a symmetrical bell-shaped curve¹³ if the rate can be reduced to zero by high substrate concentrations. This prediction agrees with experimental findings¹⁴.

Another mechanism of substrate inhibition may occur if there is a dissociable cofactor such as Mg^{++} which can combine with the substrate. Increased substrate concentration may inhibit by removing the cofactor.

Inhibitors. Two types of inhibition are commonly encountered, competitive and noncompetitive. In the competitive type, the inhibition is reduced by increasing the concentration of substrate. Many competitive inhibitors are structural analogues of the substrate, suggesting that the inhibitor and the substrate combine with the same site of the enzyme. Assuming that the inhibitor can react reversibly with the enzyme so as to prevent it combining with its substrate, it can be derived that, on the basis of mechanism (1):

$$(3) \quad v = \frac{V[S]}{K_s(1 + [I]/K_I) + [S]}$$

where $[I]$ is the concentration of inhibitor and K_I is the dissociation constant of the enzyme-inhibitor compound. V and K_s are the values obtained in the absence of the inhibitor.

In a case of noncompetitive inhibition, the amount of inhibition is independent of the concentration of substrate and depends only on the concentration of inhibitor. An equation to fit this can be derived by assuming that the inhibitor combines reversibly and equally readily with both the enzyme and the enzyme-substrate compound:

$$(4) \quad v = \frac{V[S]}{(K_s + [S])(1 + [I]/K_I)}$$

This mechanism suggests that a noncompetitive inhibitor does not combine with the active center of the enzyme responsible for combination with the substrate.

It should be noted that, in competitive inhibition, the inhibitor increases the apparent MICHAELIS constant without affecting the maximum velocity, whereas in noncompetitive inhibition the inhibitor decreases the maximum velocity without changing the MICHAELIS constant.

A third and less common type of inhibition is that in which both the maximum velocity and the MICHAELIS constant are reduced to a similar extent, so that there is no change in the ratio K_s/V as evaluated from the plots of Table 13. This type of inhibition has been termed uncompetitive and is illustrated by the action of azide on the oxidized form of cytochrome oxidase¹⁵. The appropriate equation is based on the assumption that the inhibitor combines only with the enzyme-substrate compound:

$$(5) \quad v = \frac{V[S]}{K_s + [S](1 + [I]/K_I)}$$

Plotting inhibition data. The different types of inhibition can be clearly differentiated by using any of the substrate plots of Table 13 and thus determining the effect of the inhibitor on the apparent K_s or V . Examples are shown in Figure 5 (page 468). K_I can be evaluated from the quantitative nature of this effect. To show that the appropriate equations are satisfactorily obeyed it is necessary

either to obtain the same value of K_I for more than one concentration of inhibitor or to plot data for a series of inhibitor concentrations according to the plot shown in Figure 6 above. If a straight line is obtained and the value of K_I agrees with that expected from the Figure 5 plot, it is valid to conclude that the appropriate equation is satisfactorily obeyed. In cases of competitive inhibition it is desirable to check that, when the line is produced backwards, $[I] = -K_I$ at the point where $1/v = 1/V$.

The intersections between lines for different values of $[S]$ can be used to evaluate K_I . If this method is used it is also necessary to check that equation (2) is obeyed by plotting according to one of the methods of Table 13. This need only be done with the data in the absence of inhibitor or at one inhibitor concentration.

Intermediate types of inhibition are to be expected theoretically and have, in fact, been described in careful work. These result from the inhibitor combining with both the free enzyme and the enzyme-substrate compound. Unlike strictly noncompetitive inhibition, the inhibitor has different affinities for the two forms of the enzyme. The two dissociation constants for the inhibitor (K_I from the EI compound, K_I' from the EIS compound) may be obtained from the plots of $1/v$ against $[I]$. The straight lines obtained at different values of $[S]$ intersect at $[I] = -K_I$ and $1/v = 1/V(1 - K_I/K_I')$ when they are produced backwards. The inhibition tends to be competitive if, at the intersection, $1/v > 0$, or uncompetitive if $1/v < 0$. Converse relations are obtained from plots of $[S]/v$ against $[I]$; these intersect at $[I] = -K_I$ and $[S]/v = K_s/V(1 - K_I/K_I')$.

Activators and coenzymes. When the concentration of a dissociable cofactor is varied the reaction rate usually changes according to equation (2), where $[S]$ is then the concentration of the cofactor instead of the substrate. If, however, the cofactor is somewhat firmly bound to the enzyme, the activity-concentration relation may approach two straight lines¹⁷. Several instances have been reported of coenzyme analogues inhibiting by competing with the coenzyme¹⁸.

When di- or tri-valent metal ions are required as activators it is usually found that one or more of the substrates or cofactors spontaneously combine with the activator. This can introduce serious complications into the kinetic relations.

1) SCHWIMMER and PARDEE, *Advanc. Enzymol.*, **14**, 375 (1953). 2) For a review see HELFERICH, B., in SUMNER and MYRBACK (Eds.), *The Enzymes*, vol. I, part 1, New York, 1950, page 79. 3) OGSTON, A. G., *Nature*, **162**, 963 (1948). 4) LAIDLER, K. J., *Disc. Faraday Soc.*, **20**, 83 (1955). 5) SWAIN and BROWN, *J. Amer. chem. Soc.*, **74**, 2538 (1952). 6) ROGERS and KALNITSKY, *Biochim. biophys. Acta*, **23**, 525 (1957). 7) For more extensive treatments see WILSON, P. W., in LARDY, H. A. (Ed.), *Respiratory Enzymes*, Minneapolis, 1949; FRIEDENWALD and MAENGWYN-DAVIES, in McELROY and GLASS (Eds.), *The Mechanism of Enzyme Action*, Baltimore, 1954, pages 154, 180, 191; ALBERTY, R. A., *Advanc. Enzymol.*, **17**, 1 (1956). 8) GUTFREUND, H., *Disc. Faraday Soc.*, **20**, 167 (1955). 9) ALBERTY, R. A., *Advanc. Enzymol.*, **17**, 1 (1956). 10) LAIDLER, K. J., *Trans. Faraday Soc.*, **51**, 528, 540, 550 (1955). 11) MICHAELIS and MENTEN, *Biochem. Z.*, **49**, 333 (1913); cf. HENRI, V., *C. R. Acad. Sci. (Paris)*, **135**, 916 (1902). 12) HOFSTEE, B. H. J., *Enzymologia (Amst.)*, **17**, 273 (1956); HALDANE and STERN, *Allgemeine Chemie der Enzyme*, Dresden and Leipzig, 1932. 13) FRIEDENWALD and MAENGWYN-DAVIES, in McELROY and GLASS (Eds.), *The Mechanism of Enzyme Action*, Baltimore, 1954, page 180. 14) For example see MARCUS and TALALAY, *Proc. roy. Soc. B*, **144**, 116 (1955). 15) WINZLER, R. J., *J. cell. comp. Physiol.*, **21**, 229 (1943). 16) DIXON, M., *Biochem. J.*, **55**, 170 (1953). 17) THEORELL, H., *Biochem. Z.*, **278**, 263 (1935). 18) For example see WALAAS and WALAAS, *Acta chem. scand.*, **10**, 122 (1956).

The following review of metabolism has been contributed by Professor Sir H. A. KREBS, Dr. R. B. CLAYTON, Dr. H. L. KORNBERG, Dr. J. M. LOWENSTEIN* and Dr. J. R. QUAYLE, Department of Biochemistry, University of Oxford, England. The subject has been dealt with under the following broad headings:

- General aspects of metabolism (pages 470–471)
Energy-supplying reactions (pages 472–486)
- Digestive enzymes (487–498)
Synthesis of cell constituents (pages 499–515)

This review should be read in conjunction with the section Constituents of Living Matter on pages 427–469.
A separate index to both these sections will be found on pages 520–528.

General aspects of metabolism

Chemical changes taking place in living organisms are commonly referred to as *metabolism*. By far the greater part of metabolism arises directly or indirectly from the need of living cells for energy. A smaller proportion is due to the formation of new tissues in the growing organism; the synthesis of special substances such as hormones, antibodies, digestive enzymes, urea; the detoxication of drugs and other foreign substances; and the replacement of losses due to wear and tear of the body (for example of surface epithelia or of red and white blood cells).

Since all manifestations of life are accompanied by metabolic activities, the study of metabolism is a fundamental aspect of all branches of biology. It may be taken as axiomatic that all pathological events also involve metabolic changes, either qualitative or quantitative, and the study of the biochemistry of disease is therefore of the greatest importance to medicine. The concept that most diseases – those called organic – have an anatomical basis has long been established. Every anatomical change in turn has a material, that is chemical, basis and beyond the field covered by morbid anatomy there is therefore a “molecular pathology” which deals with pathological changes in terms of chemical substances and chemical reactions. A pathological tissue is liable to possess an abnormal chemical composition as well as abnormal chemical activities, and the study of these chemical abnormalities provides a closer insight into the nature of the disorder. It may also supply information about “functional” disorders where no morphological change is detectable, because not all chemical derangements are necessarily accompanied by morphological changes. In fact, at the molecular level the distinctions between organic and functional diseases are reduced to quantitative differences, organic diseases being those disorders where the molecular changes are large enough to come within the range of optical tools.

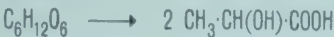
So far little more than a beginning has been made in the biochemical analysis of disease. The knowledge summarized in the following pages represents a foundation upon which molecular pathology will develop.

Energy metabolism

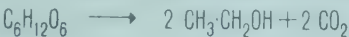
The need for energy springs from the fact that living matter is a thermodynamically unstable system which cannot be maintained unless energy is continuously added. Moreover, living matter is constantly engaged in performing various kinds of work, such as movement, chemical syntheses and transporting substances against concentration gradients. Activities of this kind cannot take place unless there is a supply of energy. Warm-blooded organisms need energy also to maintain the body temperature.

Energy is obtained by the degradation of foodstuffs. In higher organisms the overall effect of this degradation is essentially an oxidation of organic substances to carbon dioxide and water. This overall effect is the sum of many hundreds of separate chemical reactions many of which are now known in considerable detail.

Energy can also be obtained in the absence of air, i.e. anaerobically, by certain special degradation reactions of glucose and other hexoses. These are usually referred to as “fermentations” or “glycolysis”. The only form of fermentation which occurs in animal tissues is the lactic acid fermentation, by which one molecule of glucose is split into two molecules of lactic acid:



Microorganisms possess many forms of fermentation, among which the most important is the alcoholic fermentation:



The energy made available by fermentations is only a small fraction of that liberated by the oxidation of sugar. The complete oxidation of one mole of glucose yields about 686 kcal of free energy, whilst the fermentation of the same amount of glucose to lactic acid yields about 45 kcal. Thus to obtain the same amount of energy by fermentation about 15 times more glucose has to be decomposed.

* Present address: Graduate Department of Biochemistry, Brandeis University, Waltham, Mass., U.S.A.

Table 1 Rate of respiration (QO2) of animal tissues*

Representative values, measured on isolated tissues, usually slices suspended in glucose-saline medium at 38–40° C. Unless otherwise stated the data refer to rat tissues. For further data see 1

Tissue	QO2	Tissue	QO2
Kidney cortex	–25	ROUS sarcoma (chicken) ..	5
Kidney medulla	– 8	FLEXNER's carcinoma ..	8
(guinea pig)		Erythrocytes	0.6
Liver	–13	White blood cells	9
Brain cortex	–12	Thrombocytes	7
Brain white matter	– 6	Bone marrow, red	–10
Retina	–30	Adipose tissue**	0.5
Spleen	–12	Connective tissue	1
Lung	– 8	(renal capsule, goat)	
Submaxillary gland ...	–12	Cartilage (costal)	0.5
Pancreas	– 4	Skin (newborn rat)	1
Intestinal mucosa	–12	Striated muscle:	
Colonic mucosa	–10	diaphragm	7
Adrenal gland	–10	– gastrocnemius	3
Pituitary gland	–12	– breast muscle	40
Thymus gland	– 5	(pigeon, minced)	
Thyroid (guinea pig) ..	– 8	Smooth muscle	4
Testis	–10	(gizzard, pigeon)	
JENSEN's sarcoma	–11	Cardiac muscle	–18
		(sheep, minced)	

* The magnitude of respiration and fermentation is commonly expressed by the “metabolic quotients” which are defined as follows:

$$Q_{O_2} = \frac{\text{microliters of } O_2 \text{ used}}{\text{milligrams dry weight} \times \text{hours}}$$
$$Q_{CO_2} = \frac{\text{microliters of } CO_2 \text{ used or produced}}{\text{milligrams dry weight} \times \text{hours}}$$
$$Q_{\text{lactic acid}} \text{ or } Q_L = \frac{\text{microliters of lactic acid formed}}{\text{milligrams dry weight} \times \text{hours}}$$

The disappearance of a substance is usually indicated by a negative sign, the formation by a positive sign. Anaerobic and aerobic conditions are denoted by the superscripts N2 and O2, e.g.: QL^{N2}, QL^{O2}

A nongaseous substance like lactic acid is treated as if it were a gas on the assumption that 1 millimole is equivalent to 22,400 µl of gas. The reasoning in favor of this somewhat unusual connotation is that many of the measurements have been made by gasometric methods even when a substance like lactic acid is not a gas. Lactic acid production is usually measured in the presence of bicarbonate and the formation of acid is therefore followed by the production of an equivalent amount of CO2. Some authors prefer to express the amounts metabolized in micromoles. To convert micromoles into microliters, multiply micromoles by 22.4.

The following calculation translates the Q values into quantities which can be readily understood and which illustrate the high intensity of the metabolism of some cells. Since 1 milligram of lactic acid is equivalent to 250 µl of CO2, a QL value of 25 means that the material produces 10% of its own dry weight of lactic acid per hour. Since 1 µl occupies roughly the space of 1 mg of tissue, and since the ratio of wet weight to dry weight is of the order of 5, a QO2 value of 5 means that the tissue uses about its own volume of oxygen per hour.

** Calculated for dry weight less ether-soluble matter.

1) KREBS and JOHNSON, *Tab. biol. (Amst.)*, 19, 100 (1948), and ALBRITTON, E. C. (Ed.), *Standard Values in Nutrition and Metabolism*, Philadelphia, 1954.

Table 2 Rate of anaerobic lactic acid fermentation ($Q_{\text{lactic acid}}^{\text{N}_2}$) in animal tissues*

Representative values, measured on isolated tissues, usually slices suspended in glucose-saline medium at 38–40°C. Unless otherwise stated the data refer to rat tissues. For further data see ¹

Tissue	$Q_L^{\text{N}_2}$	Tissue	$Q_L^{\text{N}_2}$
Kidney cortex	3	Testis	8
Kidney medulla	28	JENSEN's sarcoma	32
(guinea pig)		ROUS sarcoma (chicken) .	30
Liver	3	FLEXNER's carcinoma ...	30
Brain cortex	18	Erythrocytes	0.35
Retina	88	White blood cells	22
Retina (pigeon)	180	(polymorphonuclear, rabbit)	
Spleen	8	White blood cells	22
Lung (rat embryo)	10	(mononuclear, rabbit)	
Submaxillary gland	5	Thrombocytes	26
Pancreas (rabbit)	3.5	Bone marrow, red	21
Intestinal mucosa	14	Adipose tissue**	0.7
Adrenal gland	4	Cartilage (costal)	1.5
Pituitary gland	13	Skin (newborn rat)	7
Thymus gland	8	Embryo	12

* See footnote to Table 1.
** Calculated for dry weight less ether-soluble matter.
¹ KREBS and JOHNSON, *Tab. biol. (Amst.)*, **19**, 100 (1948), and ALBRITTON, E. C. (Ed.), *Standard Values in Nutrition and Metabolism*, Philadelphia, 1954.

In most tissues of higher organisms, lactic acid fermentation is low in the presence of oxygen, but may be high in the absence of oxygen. The suppression of fermentation by oxygen, first observed by PASTEUR in yeast cells, is known as the PASTEUR effect.

Cell metabolism

The metabolism of the whole body is the result of the metabolic activities of the component tissues. Within the last 30 years methods have become available for the study of the metabolic activities of isolated tissues and organs. In particular, measurements have been made of the rate of respiration and lactic acid fermentation of many types of cells and tissues. A few representative figures for animal tissues are given in Tables 1 and 2.

There are wide variations in the metabolic activities of different materials. The highest rates of respiration and fermentation are found among microorganisms. *Azotobacter*, for example, at 38°C can give Q_{O_2} values of over 8000, and rates of 100–200 are common among bacteria. Anaerobic fermentation rates in microorganisms reach figures up to 400. The maximum rate of lactic acid production in muscle can probably reach $Q_L^{\text{N}_2}$ values of well over 100 for short periods. Avian retina gives the highest continuous rate of lactic acid production among animal tissues ($Q_L^{\text{N}_2}$ = 180 in pigeon retina).

Low metabolic rates are generally found in tissues of relatively low physiological activity. This is true for resting glands or muscle and in particular for tissues whose function, like that of connective tissue or bone, is largely structural or, like that of adipose tissue, is concerned with the storage of metabolically inert material.

The rates of respiration and fermentation increase with temperature, like the majority of other chemical reactions. At a critical temperature – in the case of the warm-blooded animal at about 40°C, in the case of cold-blooded animals somewhat below this temperature – a further rise in temperature reduces metabolism. In exceptional cases, those of the thermophilic bacteria, the critical temperature may be as high as 80°C.

Among the factors which affect energy production in the intact warm-blooded animal, body size has long been recognized as being of major importance. The differences in the oxygen consumption of intact animals of different size are not exactly reflected in the rates of respiration of individual tissues. In general, the tissues of larger species have a somewhat lower metabolism than the tissues of smaller species, but the differences between the Q_{O_2} values of, for example, brain, kidney, liver, spleen and lung of different species are relatively small. The characteristic differences in the basal metabolic rate of animals of different size appear to be due mainly to differences in the resting metabolism of the musculature.

Energy-supplying reactions

The first stage in the utilization of foodstuffs either for the supply of energy or for other purposes consists of a hydrolytic breakdown of the large molecules of food to the small constituent units. Proteins are converted to amino acids, carbohydrates to hexoses, fats to glycerol and fatty acid, and nucleic acids to the constituent bases, pentoses and phosphate. This hydrolytic breakdown is commonly referred to as *digestion*. Biologically speaking, digestion results in the solubilization of the foodstuffs, a prerequisite to absorption from the intestine. Processes very similar to intestinal digestion also occur in most tissues when reserve materials are mobilized to serve as a source of energy, or when damaged tissues are “autolyzed”.

Digestion is brought about by the combined action of many specific enzymes each dealing with the hydrolysis of one com-

pound or of a series of closely related compounds. The basic properties of these enzymes are described on pages 487–498.

1. Intermediary stages of carbohydrate degradation

Hexoses formed by digestion in the intestinal tract are absorbed and reach the various tissues through the blood circulation. The main reaction by which hexoses are degraded is the anaerobic fermentation to lactic acid, followed by the oxidation of the products of fermentation. An alternative pathway of oxidation exists in which glucose is oxidized without first undergoing fission to a 3-carbon compound, but this pathway, the “pentose-phosphate cycle” (see page 499), is not a major source of energy in higher animals; it probably serves mainly to supply pentoses.

Table 3 Intermediary reactions of lactic acid fermentation (glycolysis) in animal tissues (for formulas of intermediates see Figure 1)
These reactions occur in all animal tissues and in many microorganisms

No.	Intermediary reactions		Enzyme catalyzing the reaction
1	glucose + adenosine triphosphate (ATP)	→ glucose-6-phosphate + adenosine diphosphate (ADP)	Hexokinase
2	glucose-6-phosphate	→ fructose-6-phosphate	Hexose-phosphate isomerase
3	fructose-6-phosphate + ATP	→ fructose-1,6-diphosphate + ADP	Phosphofructokinase
4	fructose-1,6-diphosphate	→ dihydroxyacetone phosphate + 3-phosphoglyceraldehyde	Aldolase (zymohexase)
5	dihydroxyacetone phosphate	→ 3-phosphoglyceraldehyde	Triose-phosphate isomerase
6	2 [3-phosphoglyceraldehyde + diphosphopyridine nucleotide (DPN) + phosphate]	→ 1,3-diphosphoglyceric acid + DPNH ₂]	Triose-phosphate dehydrogenase
7	2 [1,3-diphosphoglyceric acid + ADP]	→ 3-phosphoglyceric acid + ATP]	Phosphoglycerokinase
8	2 [3-phosphoglyceric acid	→ 2-phosphoglyceric acid]	Phosphoglyceromutase
9	2 [2-phosphoglyceric acid	→ phosphopyruvic acid + H ₂ O]	Enolase
10	2 [phosphopyruvic acid + ADP]	→ pyruvic acid + ATP]	Pyruvate kinase
11	2 [pyruvic acid + DPNH ₂]	→ lactic acid + DPN]	Lactic dehydrogenase
	Balance:		
	glucose + 2 ADP + 2 phosphate	→ 2 lactic acid + 2 ATP + 2 H ₂ O	

Fig. 1 The intermediates of glycolysis formed from glucose

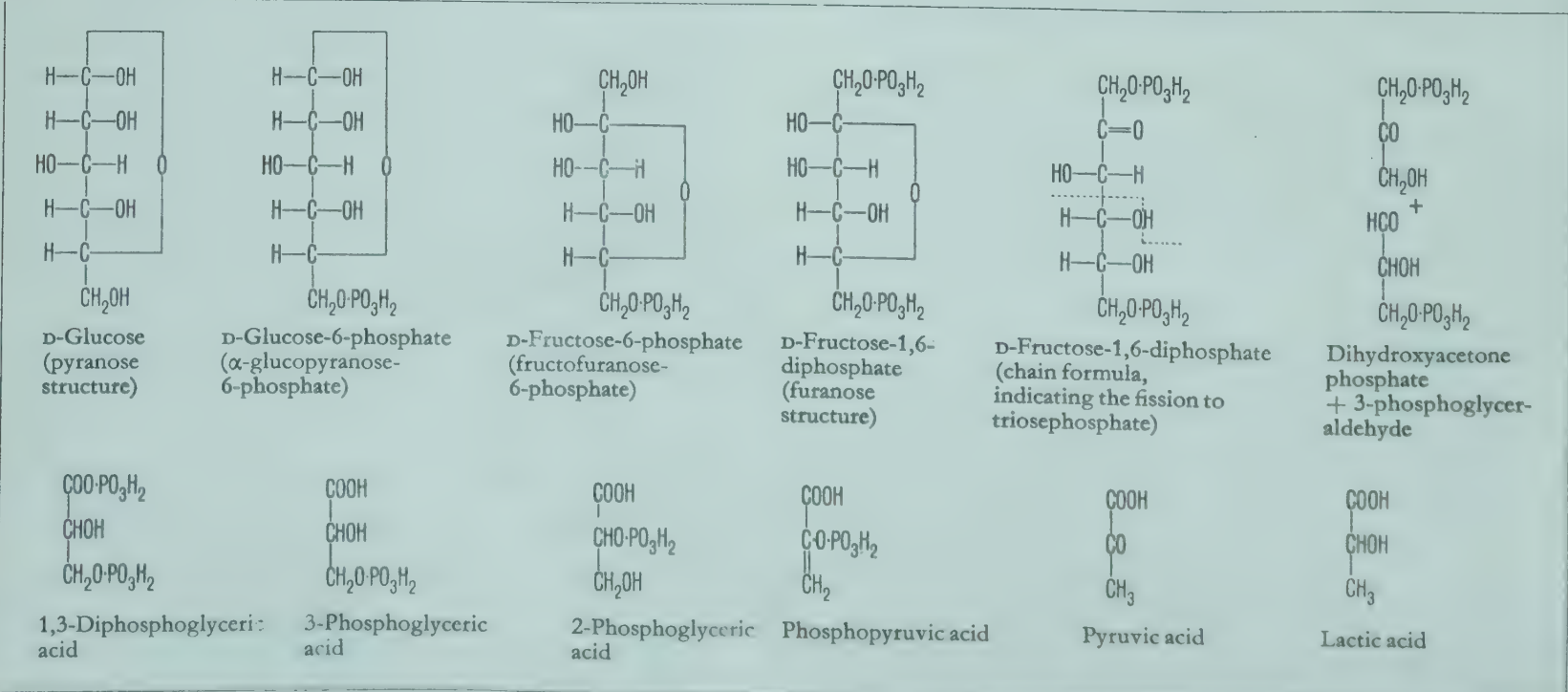


Table 4 Ancillary reactions of lactic acid fermentation in animal tissues

No.	Intermediary reactions		Enzyme catalyzing the reaction
1	glycogen + phosphate	\rightleftharpoons glucose-1-phosphate	Phosphorylase
2	glucose-1-phosphate	\rightleftharpoons glucose-6-phosphate	Phosphoglucomutase
3	fructose + ATP	\rightarrow fructose-6-phosphate + ADP	Hexokinase*
4	galactose + ATP	\rightarrow galactose-1-phosphate + ADP	Galactokinase ²
5	galactose-1-phosphate + uridine diphosphoglucose	\rightleftharpoons glucose-1-phosphate + uridine diphosphogalactose	Uridyl-transferase ³
6	uridine diphosphogalactose	\rightleftharpoons uridine diphosphoglucose	Galacto-waldenase ³
7	uridine diphosphoglucose + pyrophosphate	\rightleftharpoons uridine triphosphate (UTP) + glucose-1-phosphate	Pyrophosphorylase ⁴
8	fructose + ATP	\rightarrow fructose-1-phosphate + ADP	Fructokinase (ketohexokinase) ⁵
9	fructose-1-phosphate	\rightleftharpoons dihydroxyacetone phosphate + glyceraldehyde	Aldolase ⁵
10	glyceraldehyde + ATP	\rightarrow 3-phosphoglyceraldehyde	Triokinase ⁵

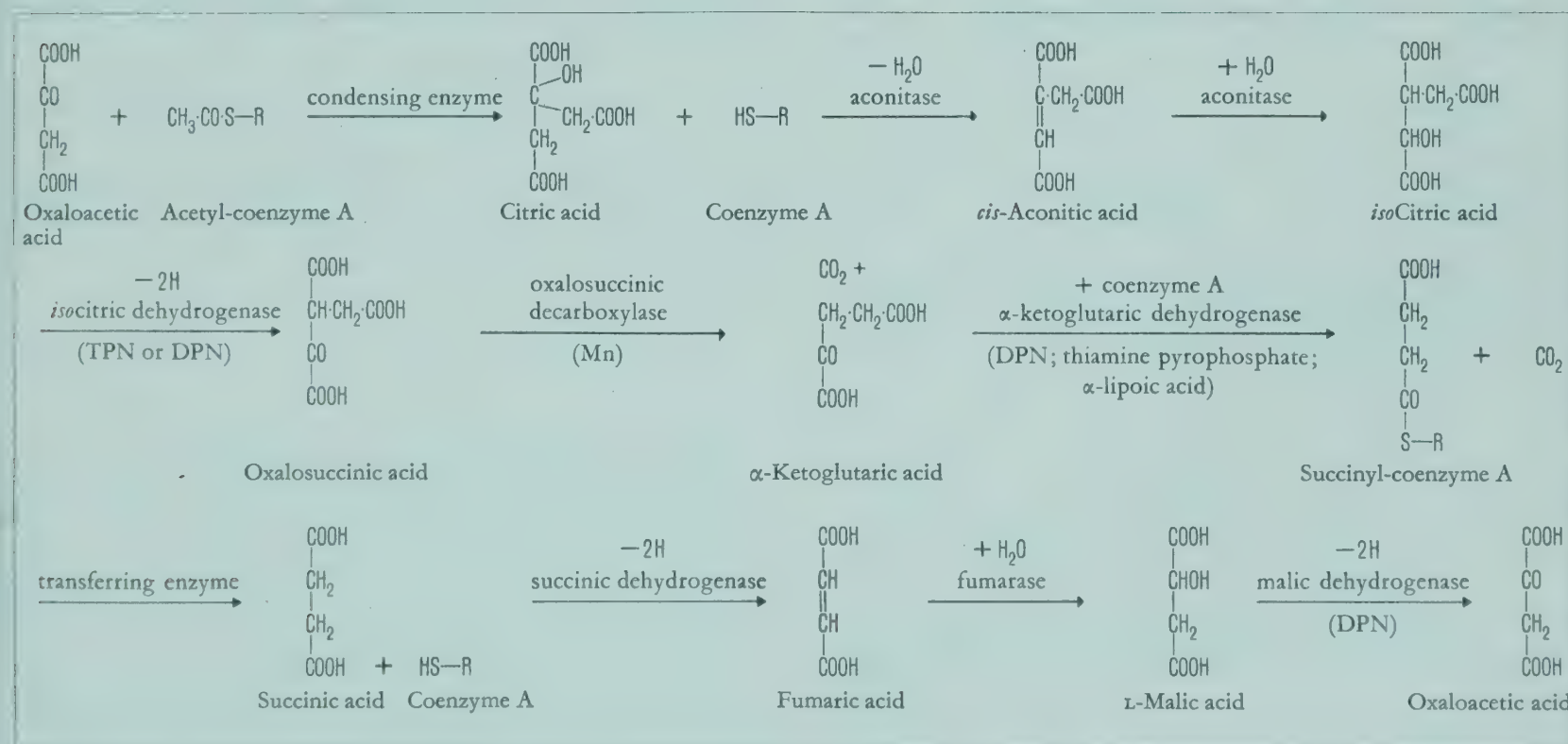
* Hexokinase reacts similarly with many other hexoses, e.g. mannose, 2-deoxyglucose.¹

1) Cf. SOLS and CRANE, *J. biol. Chem.*, **210**, 581 (1954). 2) TRUCCO et al., *Arch. Biochem.*, **18**, 137 (1948). 3) LELOIR, L. F., *Arch. Biochem. Biophys.*,

33, 186 (1951); KALCKAR et al., *Nature*, **172**, 1038 (1953); KALCKAR and MAXWELL, *Biochim. biophys. Acta*, **22**, 588 (1956). 4) MUNCH-PETERSEN et al., *Nature*, **172**, 1036 (1953). 5) LEUTHARDT et al., *Helv. chim. Acta*, **36**, 227 (1953); HERS and KUSAKA, *Biochim. biophys. Acta*, **11**, 427 (1953).

Fig. 2 The individual stages of the tricarboxylic acid cycle

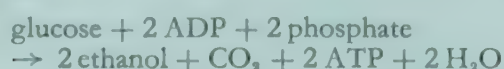
The names of the enzymes are given above the arrows, those of the coenzymes required below the arrows



Anaerobic lactic acid fermentation (glycolysis). The intermediary reactions of the lactic acid fermentation are given in Table 3. The changes of the carbon skeleton are summarized in Figure 1. The alcoholic fermentation of yeasts, molds, other microorganisms and plants follows essentially the same pathway except that reaction 11 (Table 3) is replaced by the following two reactions:

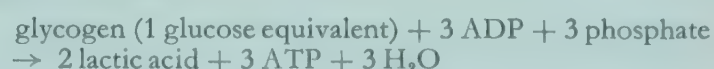


The balance reaction of the alcoholic fermentation (reactions 1-10 of Table 3, plus the above two reactions occurring twice each) is thus:



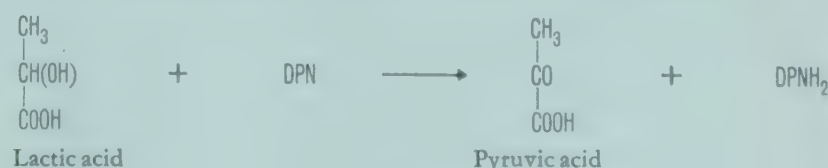
Reactions related to the lactic acid fermentation are shown in Table 4. Some of these reactions are concerned with the fermentation of other starting materials such as glycogen, fructose or

galactose. When glycogen (or starch) is the starting material the balance reaction is

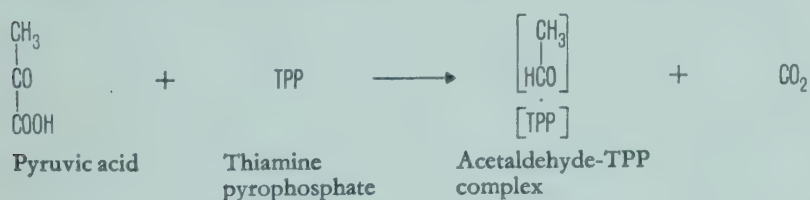


Oxidation of carbohydrate. As a rule, sugars are not oxidized as such but only after fermentation to lactic acid or triose-phosphate. As already mentioned, the alternative pathway of glucose oxidation, the pentose-phosphate cycle (see page 499), appears to be of limited significance as an energy-supplying mechanism.

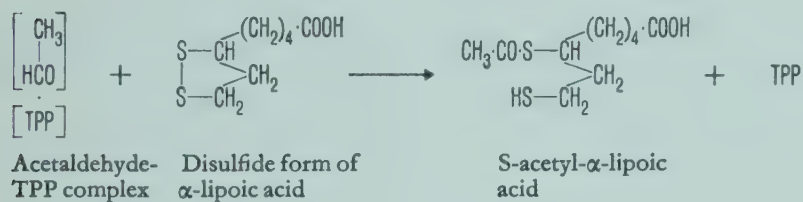
Lactic acid is first converted into acetyl-coenzyme A via pyruvic acid. The intermediary stages are assumed to be as follows:



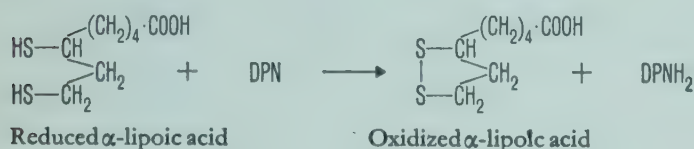
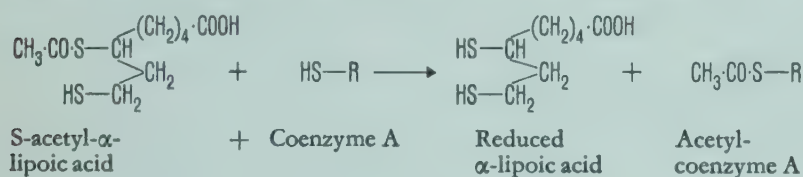
The second step is assumed to be a reaction between pyruvate and thiamine pyrophosphate (TPP) in which an acetaldehyde-TPP complex is formed and CO_2 liberated:



In the succeeding reaction the aldehyde-TPP complex reacts with the disulfide form of α -lipoic acid in such a manner that the aldehyde group of the complex is oxidized to a carboxyl group and the disulfide reduced to the dimercaptan; further the nascent carboxyl and one of the nascent thiol groups condense to form S-acetyl- α -lipoic acid:



In the next stage the acetyl group is transferred from α -lipoic acid to coenzyme A, with the formation of reduced lipoic acid and acetyl-coenzyme A. The reduced lipoic acid is reoxidized by interaction with DPN, catalyzed by lipoic acid dehydrogenase:



The sum of the last four reactions is:

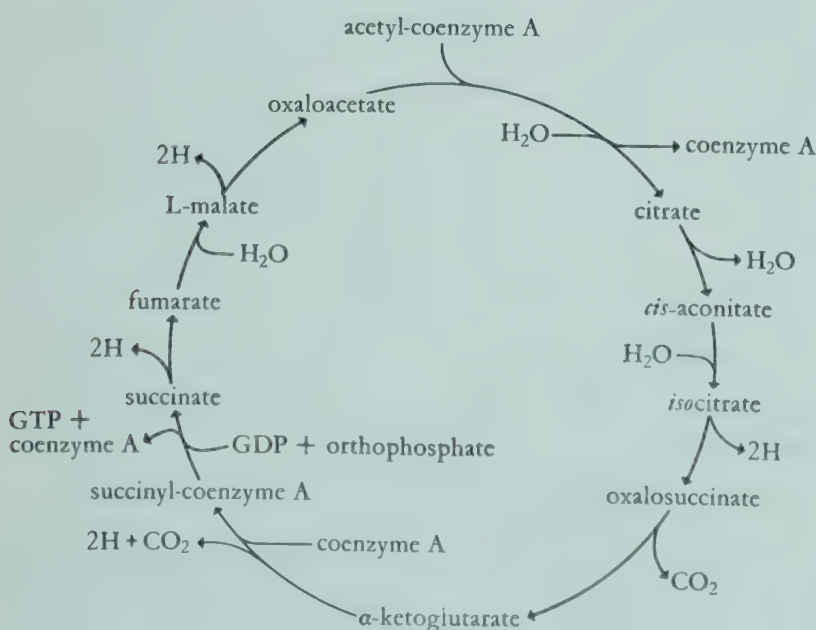
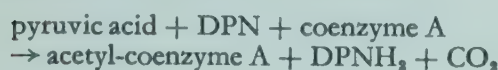


Fig. 3 The tricarboxylic acid cycle

Substances which enter the cycle (coenzyme A, H_2O) after the initial condensation of 1 molecule of acetyl-coenzyme A and 1 molecule of oxaloacetate are written inside the cycle; substances which arise are written outside. During one turn of the cycle, one acetic acid equivalent is completely oxidized. The four pairs of H atoms which arise react ultimately with O_2 to form water (for further details see KREBS, H. A., *Harvey Lect.*, **44**, 165 (1949-50), and KREBS, H. A., in GREENBERG, D. M. (Ed.), *Chemical Pathways of Metabolism*, vol. I, New York, 1954, page 109).

Analogous reactions probably occur whenever α -ketonic acids are oxidized. α -Ketonic acids arise in particular from α -amino acids; α -ketoglutarate is also formed during the tricarboxylic acid cycle.

Acetyl-coenzyme A is oxidized to completion by the tricarboxylic acid cycle (also referred to in the literature as the "citric acid cycle" or "KREBS cycle"). This cycle is initiated by a condensation of acetyl-coenzyme A and oxaloacetate leading to citrate. Citrate undergoes a series of reactions which, on balance, are oxidative and in which other tricarboxylic acids and dicarboxylic acids arise. They lead eventually to the regeneration of oxaloacetate which thus becomes available for another turn of the cycle. This means that oxaloacetate reacts after the manner of a catalyst. The hydrogen atoms arising in the course of the cycle react ultimately with molecular oxygen to form water, and the overall effect of one turn of the cycle is therefore:

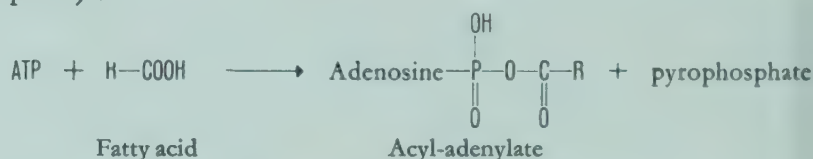


The component reactions of the cycle are given in Figure 2. The cycle itself is shown diagrammatically in Figure 3.

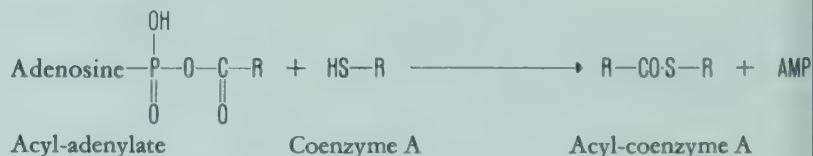
2. Oxidative degradation of fat

Fats are not oxidized in the ester form in which they are deposited in tissues and present in foods. Prior to oxidation fat is hydrolyzed to free fatty acids and glycerol, a reaction catalyzed by lipases or esterases.

The oxidation of the free fatty acids is initiated by a reaction which results in the attachment of the fatty acid radical to the sulfur atom of coenzyme A. This reaction requires the participation of ATP and of specific enzyme systems now named "thiokinases". Two stages of the reaction have been identified. The first leads to the formation of an adenylyl fatty acid (acyl-adenosine monophosphate)²:



The second is a transfer of the acyl group from adenylyl acid to coenzyme A:



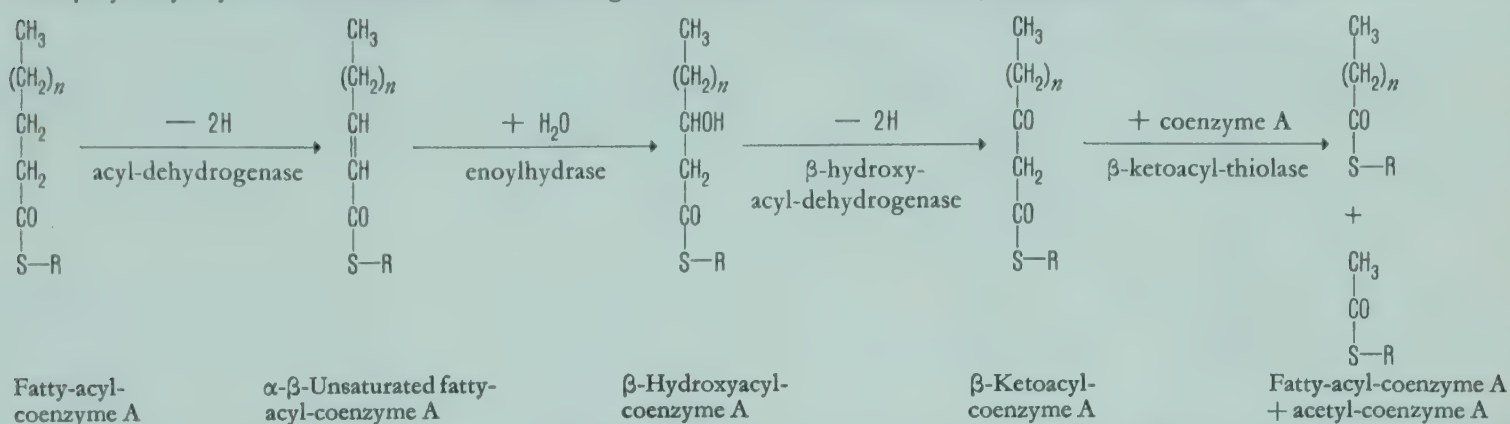
Several fatty acids, including acetic, propionic and higher fatty acids, have been shown to react in this way³. The acyl-coenzyme compounds thus formed represent the "active" forms of fatty acids which in the presence of further specific enzymes undergo a characteristic sequence of reactions, summarily referred to as β -oxidation, because the oxidation occurs at the β -carbon atom of the chain. It leads to the stepwise removal of acetic acid equivalents from the carbon chain. The intermediary enzymic reactions of this process are given in Figure 4. As shown in this scheme, β -oxidation involves four separate steps. The first is the dehydrogenation in the α - β position, the second the addition of water to the double bond and the formation of a β -hydroxy acid. The third is the dehydrogenation of the β -hydroxyl group to form a β -keto acid, the last is a "thiolysis", i.e. a fission of the carbon chain effected by the sulfhydryl group of coenzyme A. It results in the formation of one molecule of acetyl-coenzyme A and an acyl-coenzyme A derivative shorter than the original chain by two carbon atoms. The shortened chain repeatedly undergoes the same sequence of reactions until the whole fatty acid chain is reduced to a fragment of less than four carbon atoms. In the case of chains with even numbers of carbon atoms the last fragment is acetyl-coenzyme A, in the case of those with uneven numbers it is propionyl-coenzyme A.

The great majority of naturally-occurring fatty acids contain an even number of carbon atoms and therefore yield acetyl-coenzyme A as the only product. The propionyl-coenzyme A formed from uneven chains is known to enter a CO_2 -fixation reaction leading to succinic acid (see page 502).

The sequence of reactions by which fatty acids are oxidized has been referred to as the "fatty acid cycle". It is not a cycle in the strict sense since the starting material is not regenerated by a full

Fig. 4 β -Oxidation of fatty acids

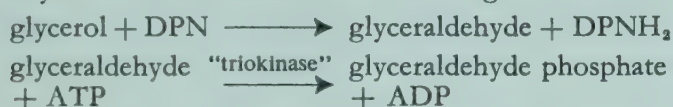
The nomenclature of the enzymes has been internationally proposed⁴. Acyl-dehydrogenase is a flavoprotein, β -hydroxyacyl-dehydrogenase requires DPN. All four reactions are reversible. The β -hydroxyacyl-coenzyme A compounds are optically active and belong to the D-series, in contrast to the free β -hydroxybutyrate in blood and urine which belong to the L-series. The latter arises by reduction of free acetoacetate⁶.



turn of the "cycle". What happens is a periodic repetition of the same *types* of reaction, but not of the same reactions. This is shown diagrammatically in Figure 5, from which it can be seen that the mechanism is a "spiral" rather than a "cycle".

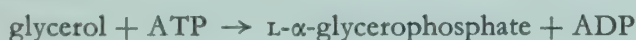
The enzymic mechanism of the formation and degradation of unsaturated fatty acids is not yet known in any detail. It is possible that unsaturated fatty acids (among which oleic acid is the most common) are reduced to the saturated fatty acids before they are degraded.

Glycerol, the second constituent of neutral fats, is known to be convertible into carbohydrate in mammalian liver and the evidence suggests that this involves the formation of triosephosphate from glycerol⁶. Triosephosphate may be formed from glycerol by two pathways. The first consists of the following two reactions:

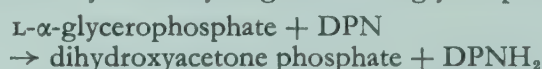


The occurrence of both reactions has been demonstrated⁷.

Alternatively the primary step may be a phosphorylation of glycerol⁸:

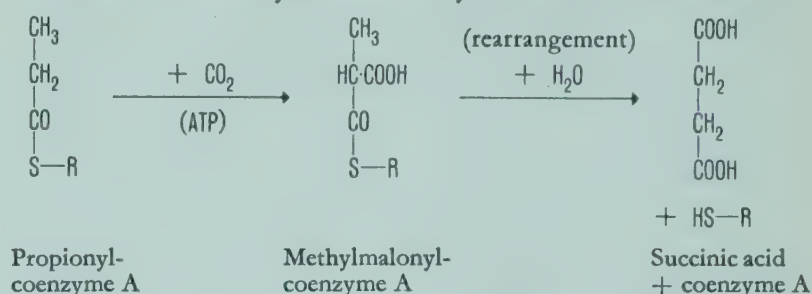


followed by the dehydrogenation of glycerophosphate:

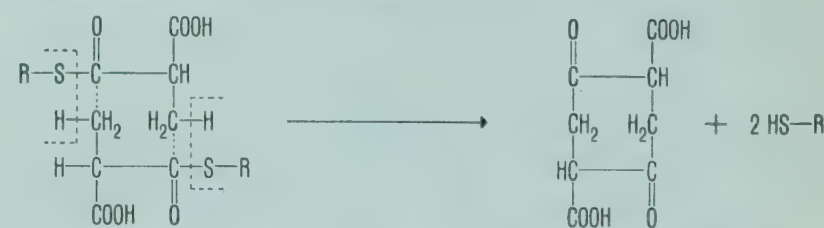


The triosephosphate formed from glycerol subsequently joins the reactions of triosephosphate arising from sugars.

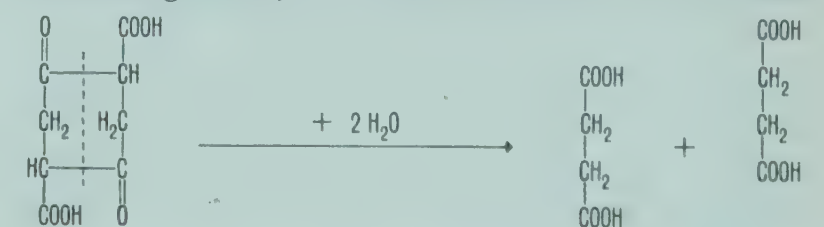
Formation of succinic acid from propionyl-coenzyme A. As already mentioned, the propionyl-coenzyme A formed from fatty acids with uneven carbon chains yields succinic acid. This involves a CO_2 -fixation reaction recently discovered by OCHOA and co-workers⁹:



The conversion of methylmalonyl-coenzyme A to succinic acid by simple intramolecular rearrangement is difficult to visualize. FESSLER¹⁰ has suggested that two molecules may react to form a condensation product, as follows:



If this condensation product is split hydrolytically according to the following scheme, two molecules of succinic acid are formed:



Terminal oxidation of fat. The degradation reactions of fat so far considered bring about an incomplete oxidation of fatty acids and glycerol. The main product of this incomplete oxidation is acetic acid in the form of acetyl-coenzyme A. The only other product is succinic acid, which arises from the three terminal carbon atoms of the fatty acid chain with uneven carbon numbers. Since fatty acids with uneven carbon numbers are uncommon in nature the total amount of succinate arising from fat is normally very small. Such fatty acids are uncommon because fatty acid chains are usually synthesized from 2-carbon units.

Acetyl-coenzyme A and succinate are oxidized to completion by the reactions of the tricarboxylic acid cycle described on page 474.

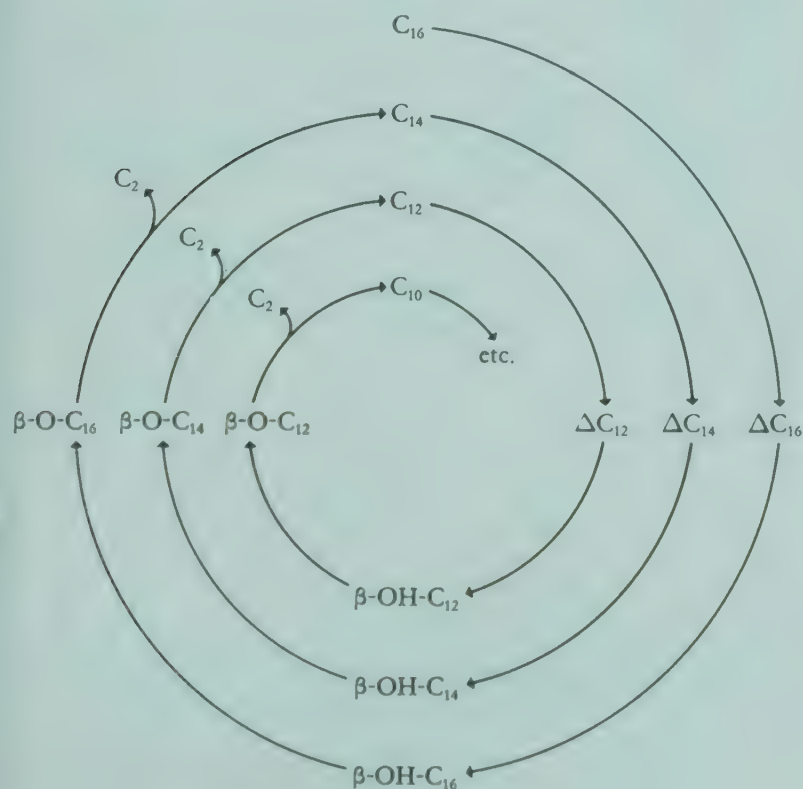
Ketosis. In ketosis due to starvation or diabetes or other causes, the "ketone bodies", viz. acetoacetate ($\text{CH}_3 \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{COOH}$), β -hydroxybutyrate ($\text{CH}_3 \cdot \text{CHOH} \cdot \text{CH}_2 \cdot \text{COOH}$) and acetone

Fig. 5 Diagram of the "spiral" of fatty acid oxidation

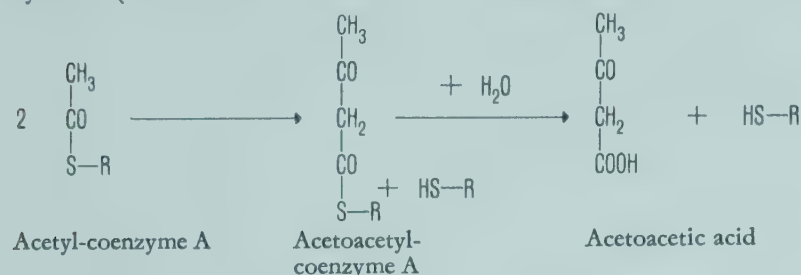
Abbreviations:

$\text{C}_2, \text{C}_4, \text{etc.}$ = fatty-acyl-coenzyme A
 $\Delta\text{C}_2, \Delta\text{C}_4, \text{etc.}$ = unsaturated fatty-acyl-coenzyme A
 $\beta\text{-OH-C}_2, \beta\text{-OH-C}_4, \text{etc.}$ = β -hydroxyacyl-coenzyme A
 $\beta\text{-O-C}_2, \beta\text{-O-C}_4, \text{etc.}$ = β -ketoacyl-coenzyme A
 C_2 = acetyl-coenzyme A

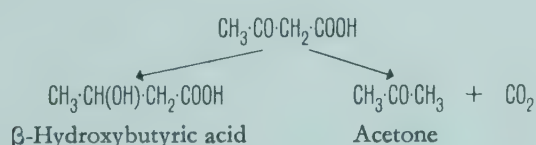
The subscripts indicate the length of the carbon chain.



($\text{CH}_3 \cdot \text{CO} \cdot \text{CH}_3$), accumulate in the tissues and body fluids. For reasons which are not yet fully understood more acetyl-coenzyme A is formed in ketosis, mainly from fatty acids, than can be oxidized through the tricarboxylic acid cycle. The surplus molecules of acetyl-coenzyme A condense in pairs to form acetoacetyl-coenzyme A which undergoes hydrolysis to free acetoacetate and coenzyme A (in liver free acetoacetate is not readily utilized):



Acetoacetate is the primary ketone body. β -Hydroxybutyrate is formed from it by reduction, acetone by decarboxylation. The latter reaction is mainly nonenzymic, and is due to the inherent instability of acetoacetate:



The older view that acetoacetate arises directly from the four terminal carbon atoms of fatty acid chains is no longer tenable in view of isotope data which prove conclusively that *most* acetoacetate is formed by the condensation of two molecules of acetyl-coenzyme A.

It follows that all substances which can form acetyl-coenzyme A, including carbohydrate and many amino acids, can be parent substances of the ketone bodies. Why ketone bodies accumulate only when acetyl-coenzyme A is formed from fatty acids and the three ketogenic amino acids, and not when it is formed from carbohydrate and other amino acids, is not clear. Since the oxidation of acetyl-coenzyme A through the tricarboxylic acid cycle requires oxaloacetate it is likely that oxaloacetate is a key substance in the control of ketosis. It has been assumed that a sufficient level of oxaloacetate for the optimal operation of the tricarboxylic acid cycle cannot be maintained unless carbohydrate is oxidized, but why this should be the case is still a matter of conjecture.

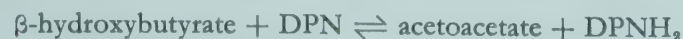
Ancillary reactions of fatty acid degradation. Some ancillary degradation reactions of fatty acids are the following.

(a) Acetoacetyl-deacylase liberates free acetoacetate from the coenzyme A derivative:



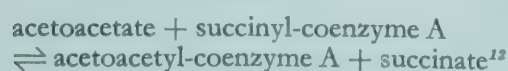
This reaction is assumed to play a role in the appearance of the ketone bodies in blood and tissues in ketosis¹².

(b) β -Hydroxybutyric dehydrogenase catalyzes the reversible interconversion of acetoacetate and β -hydroxybutyrate:

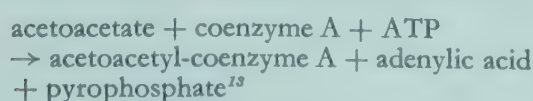


and is responsible for the formation and removal of β -hydroxybutyrate.

(c) An enzyme transferring coenzyme A reversibly between acetoacetate and succinate ("thiopherase") may initiate the breakdown of free acetoacetate:



(d) Acetoacetate breakdown can also be initiated by the reaction



This is analogous to the reaction which initiates the degradation of fatty acids (page 479) and may involve the same type of intermediary stages, i.e. the formation of acetoacetyl-adenylate.

1) Cf. LYNEN, F., *Harvey Lect.*, **48**, 210 (1952-53); GREEN, D. E., *Biol. Rev.*, **29**, 330 (1954); POPJAK and LE BRETON (Eds.), *Biochemical Problems of Lipids*, London, 1956; BEINERT et al., *Biochem. J.*, **64**, 782 (1956). 2) BERG, P., *J. biol. Chem.*,

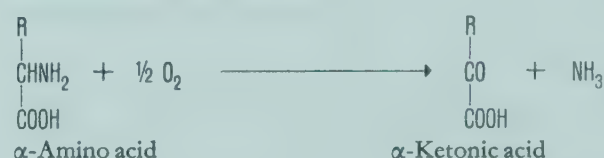
222, 991, 1015, 1025 (1956). 3) PENG, C. H. L., *Biochim. biophys. Acta*, **22**, 42 (1956); JENCKS and LIPMANN, *J. biol. Chem.*, **225**, 207 (1957); WHITEHOUSE et al., *J. biol. Chem.*, **226**, 813 (1957). 4) See *Biochem. J.*, **64**, 782 (1956). 5) LEHNINGER and GREVILLE, *Biochim. biophys. Acta*, **12**, 188 (1953). 6) ASHMORE et al., *J. biol. Chem.*, **215**, 153 (1955). 7) HERS and KUSAKA, *Biochim. biophys. Acta*, **11**, 427 (1953); WOLF and LEUTHARDT, *Helv. chim. Acta*, **36**, 1463 (1953). 8) BUBLITZ and KENNEDY, *J. biol. Chem.*, **211**, 951 (1954). 9) FLAVIN et al., *Nature*, **176**, 823 (1955). 10) FESSLER, J. H. (1956), unpublished. 11) GREEN, D. E., *Biol. Rev.*, **29**, 330 (1954). 12) STERN et al., *J. Amer. chem. Soc.*, **75**, 1517 (1953). 13) STERN and OCHOA, *J. biol. Chem.*, **191**, 161 (1951).

3. Intermediary stages of the degradation of amino acids

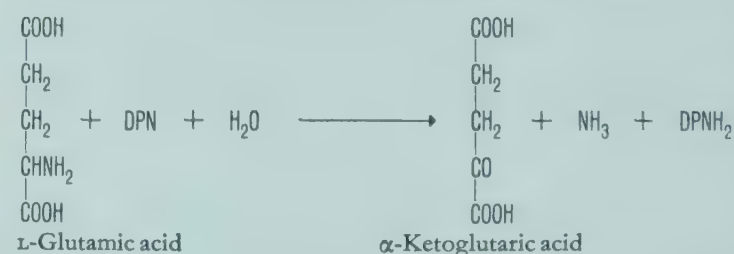
As in the case of carbohydrate and fat, the degradation of amino acids consists of two major stages. In the first stage the amino acids are converted into an intermediate which can be oxidized through the tricarboxylic acid cycle. The second or terminal stage is the tricarboxylic acid cycle. The following account is concerned with the first stage.

General degradation reactions. Some degradation reactions are common to all or several amino acids. These are (a) oxidative deamination, (b) transamination, (c) nonoxidative decarboxylation.

Oxidative deamination. The general reaction scheme of oxidative deamination is as follows:

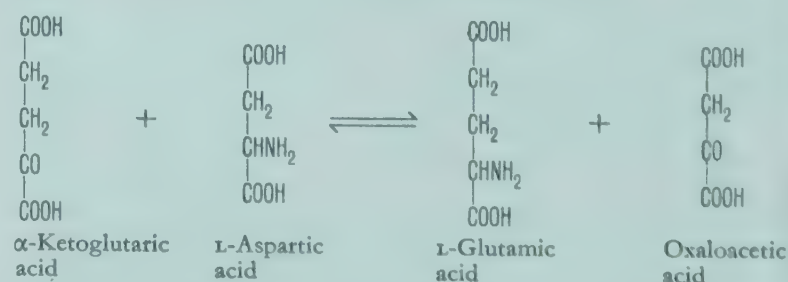


Liver and kidney contain enzymes which attack the majority of α -amino acids of both the D- and L-series in this way. In general the activity of the D-amino acid oxidases is greater than that of the L-amino acid oxidases, although D-amino acids occur very infrequently in natural products. One L-amino acid, however, reacts at a much greater rate than all other L-amino acids. This is glutamic acid, which is attacked by a specific L-glutamic acid dehydrogenase catalyzing the following reaction:



This enzyme differs from all the other enzymes bringing about oxidative deamination in animal tissues in that it transfers hydrogen to diphosphopyridine nucleotide (DPN). In the case of oxidative deamination by the other enzymes, the primary acceptor is a flavoprotein. The L-amino acid oxidases of animal tissues are comparatively weak and it is probable that deamination is generally effected by transamination of α -amino acids with α -ketoglutarate (see below) followed by the dehydrogenation of glutamate according to the above reaction.

Transamination. Transamination is a reversible reaction between amino and α -ketonic acids leading to the exchange of the amino and ketonic groups. An example is the following:



The majority of α -amino acids can replace aspartic acid in this type of reaction, according to the general scheme:

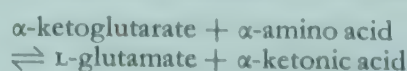


Table 5 Some transamination reactions in animal tissues¹

Reactions			Remarks
α -ketoglutarate + L- α -amino acid	\rightleftharpoons	L-glutamate + α -ketonic acid	Most α -amino acids can react in this way in liver and many other tissues
α -ketoglutarate + L-ornithine	\rightleftharpoons	L-glutamate + L-glutamic γ -semialdehyde	Involves transfer of ω -amino groups; occurs in liver ^{2,3}
glyoxylate + L-ornithine	\rightleftharpoons	glycine + L-glutamic γ -semialdehyde	
pyruvate + L-ornithine	\rightleftharpoons	L-alanine + L-glutamic γ -semialdehyde	
L-glutamine + α -keto- γ -guanidinovaleric acid	\rightleftharpoons	α -ketoglutarate + L-arginine + NH ₃	Occurs in liver ²
L-alanine + hydroxypyruvate	\rightleftharpoons	pyruvate + L-serine	Occurs in liver and kidney ⁴
α -ketoglutarate + γ -aminobutyrate	\rightleftharpoons	L-glutamate + succinic semialdehyde	Occurs in brain ⁵
α -ketoglutarate + β -alanine	\rightleftharpoons	L-glutamate + malonic semialdehyde	Occurs in brain ⁶

1) For reviews see MEISTER, A., in McELROY and GLASS (Eds.), *A Symposium on Amino Acid Metabolism*, Baltimore, 1955, page 3; MEISTER, A., *Advanc. Enzymol.*, **16**, 185 (1955). 2) MEISTER, A., *J. biol. Chem.*, **206**, 587 (1954). 3) QUASTEL and WITTY, *Nature*, **167**, 556 (1951). 4) SALLACH,

H. J., in McELROY and GLASS (Eds.), *A Symposium on Amino Acid Metabolism*, Baltimore, 1955, page 782. 5) BESSMAN et al., *J. biol. Chem.*, **201**, 385 (1953). 6) ROBERTS and BREGOFF, *J. biol. Chem.*, **201**, 393 (1953).

but the rate of reaction is by far the highest when aspartic acid is the amino-group donor. Transaminases occur in most animal tissues as well as in microorganisms and plants. Several tissues contain special types of transaminases. Some of these enzymes are listed in Table 5 above.

Transaminases readily diffuse from tissues into blood plasma when the tissue has suffered damage. This is the basis of a clinical test, the rise of the plasma level of transaminase in cardiac infarction. Pyridoxal phosphate is a prosthetic group of transaminases.

Decarboxylation. Decarboxylation of amino acids proceeds according to the following general scheme:

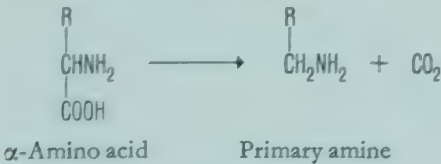


Table 6 Decarboxylation of L-amino acids¹

Most of the bacterial reactions listed below occur in the microorganisms of the intestinal tract, e.g. *Escherichia coli*, *Streptococcus faecalis* or *Clostridium* species

Amino acid	Amine formed	Occurrence of enzyme
Histidine	Histamine	Animal tissues, bacteria
Cysteic acid	Taurine	Liver
Glutamic acid	γ -Aminobutyric acid	Brain, bacteria
5-Hydroxytryptophan	5-Hydroxytryptamine (serotonin)	Animal tissues
3,4-Dihydroxyphenylalanine	3,4-Dihydroxyphenylethylamine	Animal tissues
Serine	Ethanolamine	Animal tissues ²
Lysine	Cadaverine	Bacteria
Ornithine	Putrescine	Bacteria
Tyrosine	Tyramine	Bacteria
Phenylalanine	Phenylethylamine	Bacteria
Aspartic acid	β -Alanine	Bacteria
α,ϵ -Diaminopimelic acid	Lysine	Bacteria ³

1) BLASCHKO, H., *Advanc. Enzymol.*, **5**, 67 (1945); GALE, E. F., *Advanc. Enzymol.*, **6**, 1 (1946); SCHALES, O., in SUMNER and MYRBACK (Eds.), *The Enzymes*, vol. II, part 1, New York, 1951, page 216. 2) ARNSTEIN, H. R. V., *Biochem. J.*, **48**, 27 (1951). 3) DEWEY and WORK, *Nature*, **169**, 533 (1952).

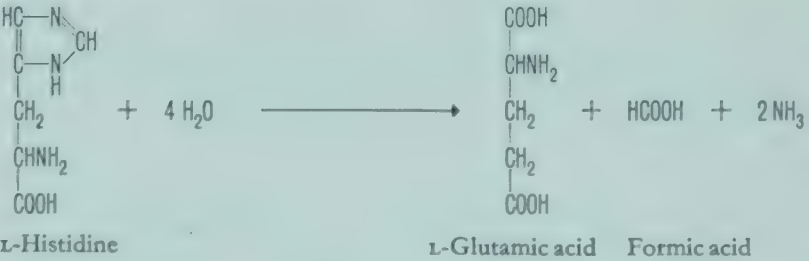
Decarboxylases occur in animal tissues and in many microorganisms, but not every amino acid can undergo decarboxylation. Reactions which have been recorded are listed in Table 6. The significance of some of the decarboxylations which occur in animal tissues lies in the supply of essential metabolites, e.g. of taurine (required for the synthesis of bile acids), of histamine and serotonin (required for the functional activities of nervous tissue) or of ethanolamine (required for the synthesis of cephalins, choline and acetylcholine). Pyridoxal phosphate is a coenzyme also in most decarboxylation reactions. A notable exception is the decarboxylation of histidine.

4. Degradation of individual amino acids¹

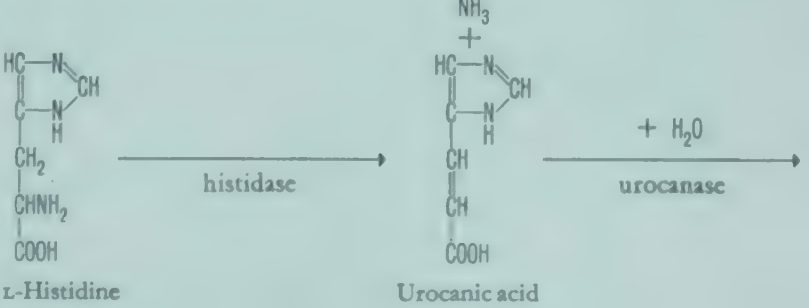
L-Glutamic acid, L-aspartic acid, L-alanine. On oxidative deamination or transamination these three amino acids yield α -ketonic acids which also occur as intermediates in the metabolism of carbohydrate; they are α -ketoglutarate, oxaloacetate and pyruvate respectively.

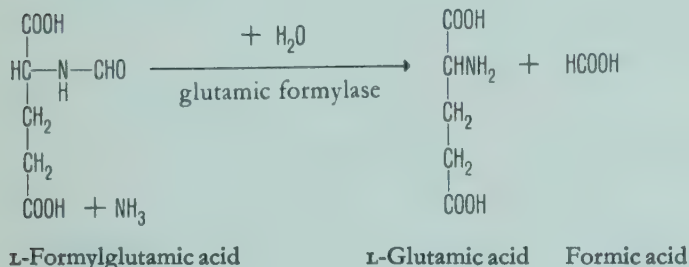
The degradation of the six amino acids **L-histidine, L-arginine, L-citrulline, L-ornithine, L-proline and L-hydroxyproline** leads in every case to glutamic acid and thence to α -ketoglutarate.

L-Histidine is converted to glutamic acid by an enzyme complex of liver tissue, formerly referred to as histidase. The overall result of the action of this complex is an hydrolysis according to the following scheme:

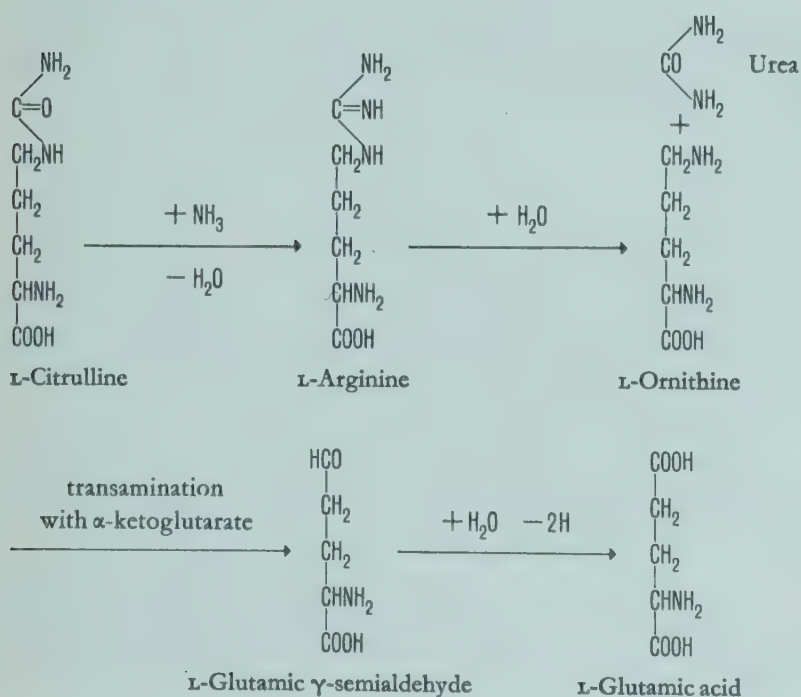


There are probably five intermediate stages. The first is the fission to ammonia and an unsaturated derivative of histidine. The other four are hydrolytic reactions, each accounting for the uptake of one molecule of water:

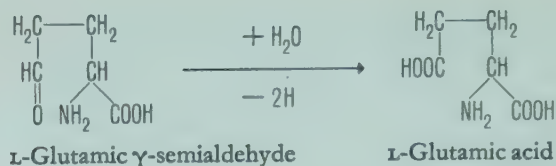




L-Citrulline and *L*-arginine are converted in liver tissue into ornithine by the reactions of the ornithine cycle (see page 516). *L*-Ornithine is known to yield glutamic γ -semialdehyde by transamination (see page 477) and the semialdehyde can form glutamic acid by dehydrogenation:


$$\begin{array}{ccc}
 \begin{array}{c} \text{CHNH}_2 \\ | \\ \text{CH}_2 \\ | \\ \text{CH}_2 \\ | \\ \text{CHNH}_2 \\ | \\ \text{COOH} \end{array} & + \frac{1}{2} \text{O}_2 \xrightarrow{\text{D-amino acid oxidase}} & \begin{array}{c} \text{CH}_2\text{NH}_2 \\ | \\ \text{CH}_2 \\ | \\ \text{CH}_2 \\ | \\ \text{CO} \\ | \\ \text{COOH} \end{array} + \text{NH}_3 \\
 \text{D-Ornithine} & & \alpha\text{-Keto-}\delta\text{-aminovaleric acid}
 \end{array}$$
$$\begin{array}{c}
 \text{H}_2\text{C}-\text{CH}_2 \\
 | \quad | \\
 \text{H}_2\text{C}-\text{CH} \\
 | \quad | \\
 \text{N}-\text{COOH} \\
 | \\
 \text{H}
 \end{array}
 \xrightarrow{-2\text{H}}
 \begin{array}{c}
 \text{H}_2\text{C}-\text{CH}_2 \\
 | \quad | \\
 \text{HC}=\text{CH} \\
 | \quad | \\
 \text{N}-\text{COOH}
 \end{array}
 \xrightarrow{+\text{H}_2\text{O}}$$

L-Proline **L-Δ¹-Pyrroline-5-carboxylic acid**

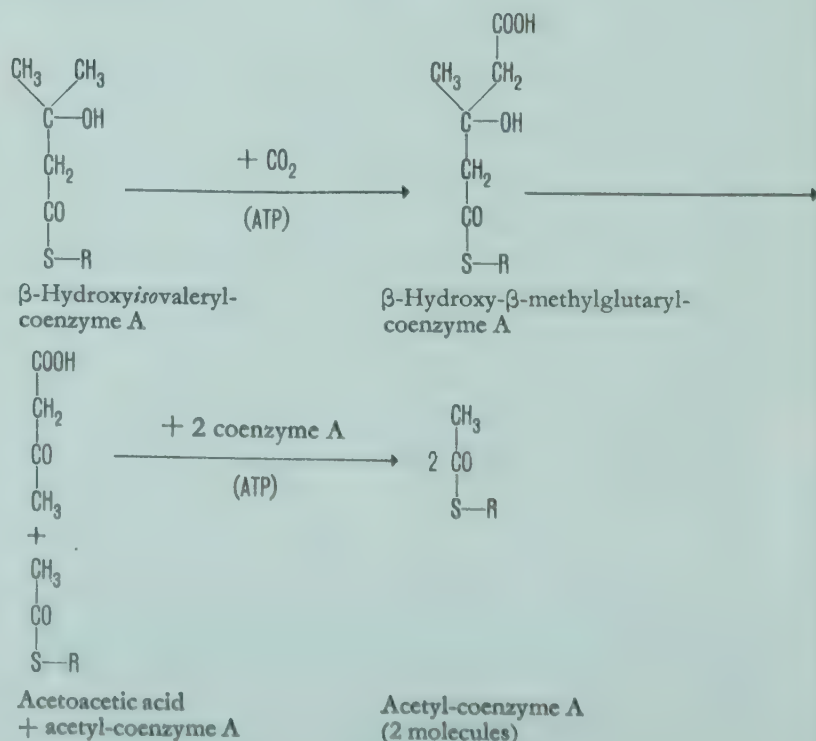
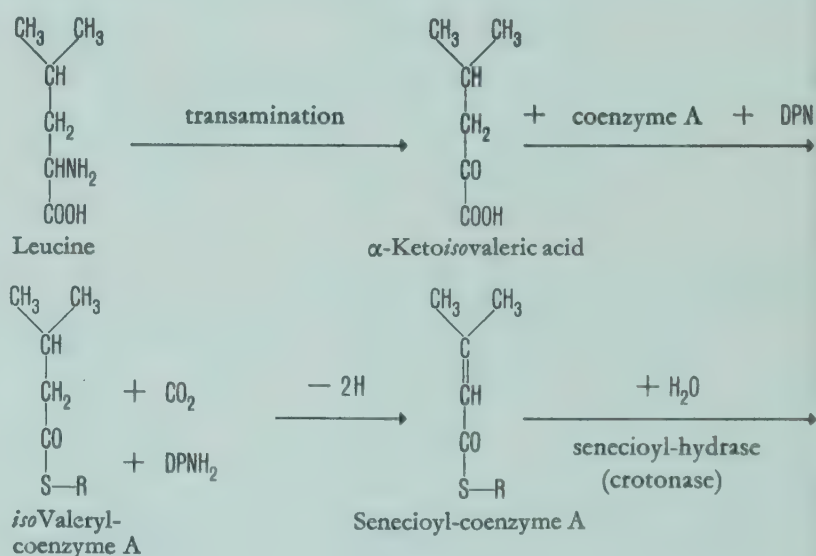


D-Proline reacts differently in mammalian liver or kidney and gives the same α -ketonic acid as D-ornithine. This is to be expected as the point of attack of D-amino acid oxidase is always the α -carbon atom.

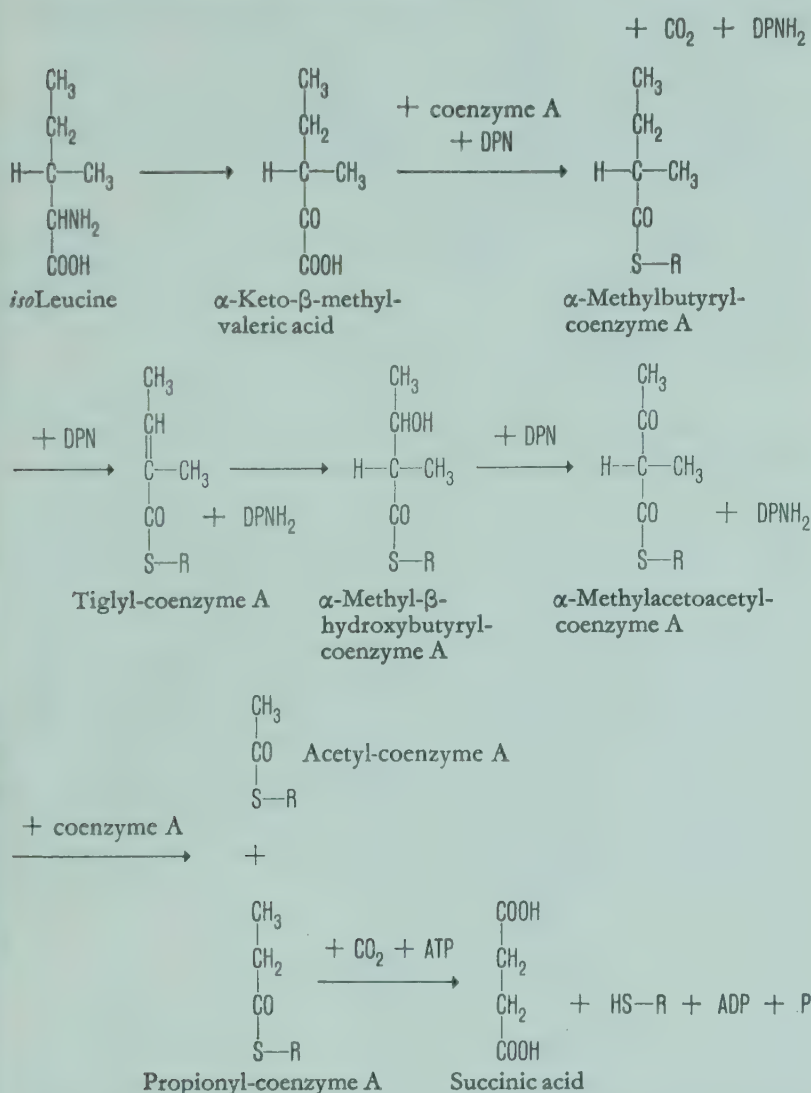
L-Hydroxyproline is known to form glutamic acid in liver and kidney but the intermediary stages of the conversion have not yet been established. It is possible that hydroxyproline is first converted into proline or a pyrrolinecarboxylic acid and shares the later stages of degradation with proline.

The degradation of the *leucines* and *valines* follows initially a common pattern. In every case transamination or oxidative deamination leads to the corresponding α -ketonic acid. This subsequently undergoes reactions analogous to those described for pyruvic acid (page 474), resulting in the formation of an acyl-coenzyme A derivative and CO_2 . The acyl-coenzyme A derivative then reacts essentially in the same way as the acyl-coenzyme A derivative of long-chain fatty acids. Special reactions – CO_2 -fixation and an aldol fission – follow in the case of leucine. The end-products are acetyl-coenzyme A and propionyl-coenzyme A, and in the case of valine probably methylmalonyl-coenzyme A. As already mentioned (page 475), both propionyl-coenzyme A and methylmalonyl-coenzyme A eventually yield succinate.

Leucine yields three molecules of acetyl-coenzyme A. The intermediate stages are as follows⁹:

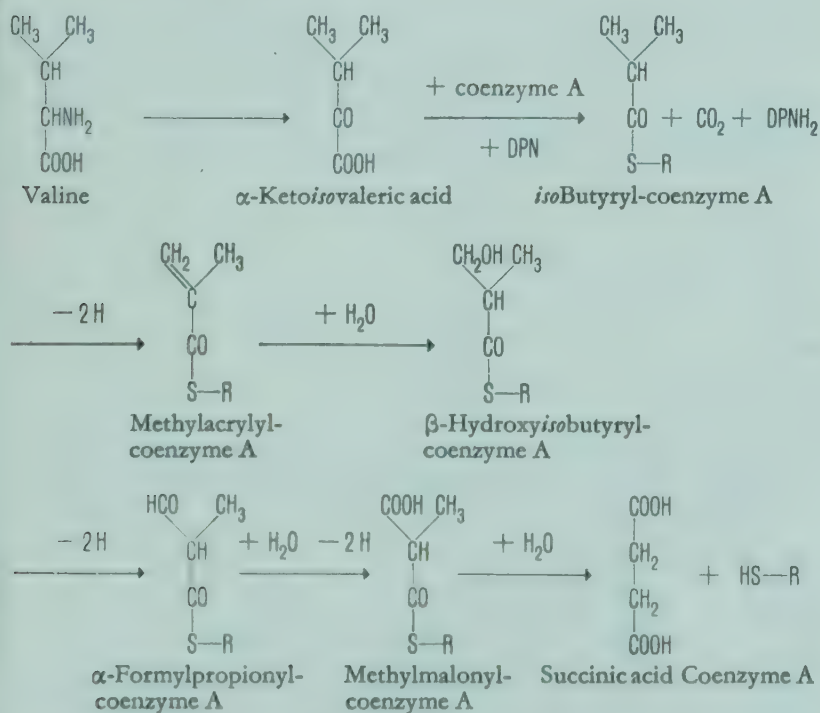


isoLeucine yields one molecule of acetyl-coenzyme A and one molecule of propionyl-coenzyme A⁴:

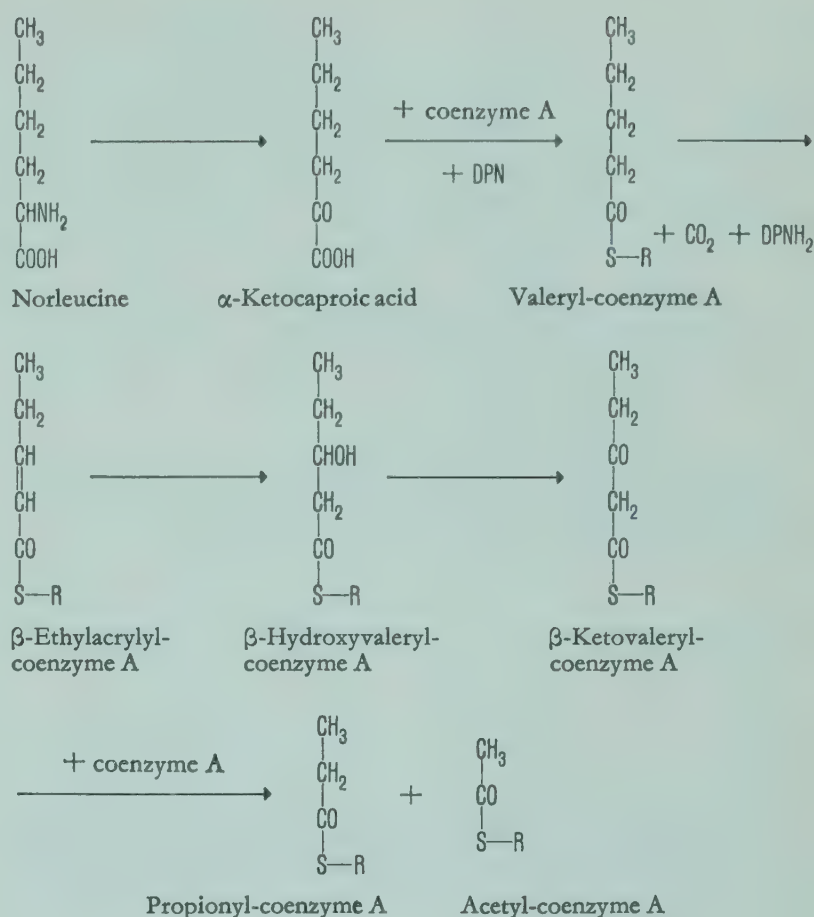


The mechanism of the last of these reactions is discussed on page 475.

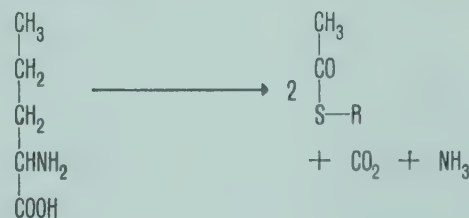
Valine is degraded by analogous reactions, as shown in the following scheme. The experimental findings support the stages up to β -hydroxyisobutyryl-coenzyme A⁵. The subsequent stages, though not yet directly demonstrated, are very probable; they are strictly analogous to the degradation reactions of the leucines and lead to methylmalonyl-coenzyme A and thence to succinic acid. What has also been firmly established is the conversion of part of the valine molecule into glucose. As succinic acid is glucogenic the proposed scheme is in accord with the facts.



Norleucine (which is not a protein constituent) has not been studied in detail, but by analogy it is expected to undergo the following sequence of reactions leading to propionyl-coenzyme A and acetyl-coenzyme A:



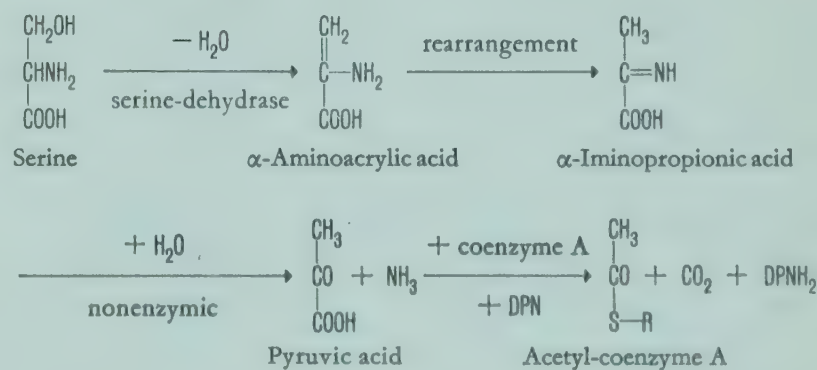
Norvaline, by the same types of reaction, forms two molecules of acetyl-coenzyme A:



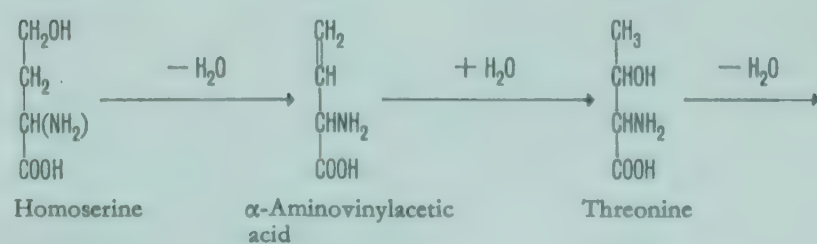
α -Aminobutyric acid by analogy forms propionyl-coenzyme A and thence succinate.

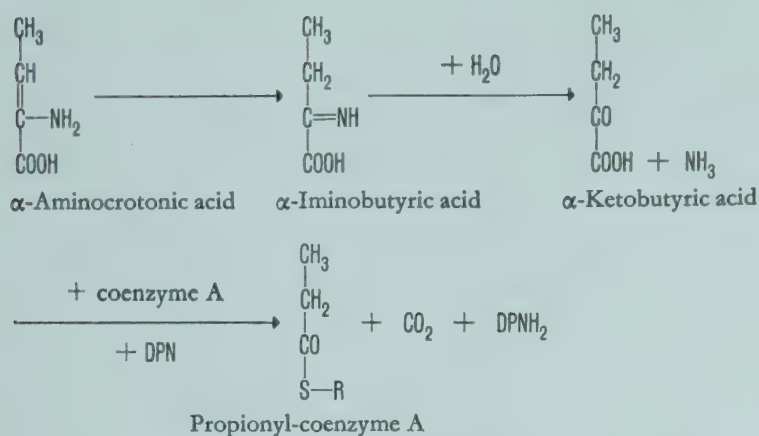
The *hydroxyamino acids* (serine, homoserine, threonine) and *glycine* react atypically in that the oxidative deamination is not the primary step.

Serine yields anaerobically ammonia and pyruvic acid in animal tissues as well as in microorganisms. The intermediate steps are assumed to be as follows⁶:

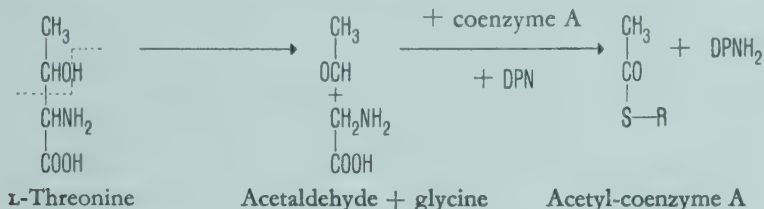


Homoserine (an intermediate in the metabolism of methionine) is known to undergo an analogous nonoxidative deamination on incubation with liver extracts, yielding α -ketobutyric acid and ammonia⁷⁻⁹:



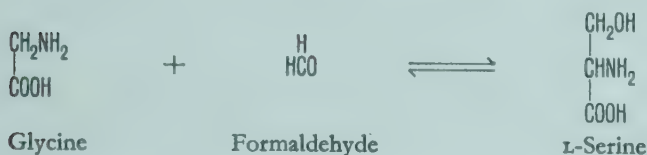


L-Threonine is degraded in animal tissues by an anaerobic fission catalyzed by an aldolase ("hydroxyamino acid aldolase")¹⁰⁻¹²:



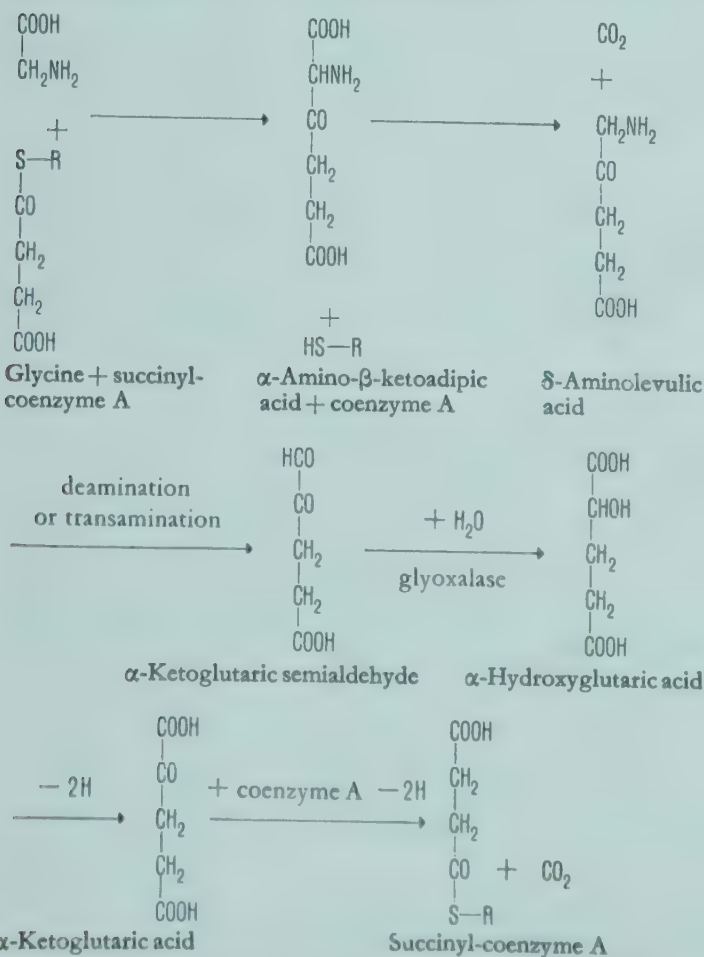
The acetaldehyde formed can be converted into acetyl-coenzyme A, whilst the glycine reacts as described later. Bacteria and molds possess enzymes which degrade threonine by reactions analogous to those of serine, yielding α -aminocrotonic acid, α -ketobutyric acid and propionic acid.

Glycine. The pathway of degradation of glycine is not yet fully clarified. One route is the conversion into serine by an aldol condensation with formaldehyde reacting in an "active form":



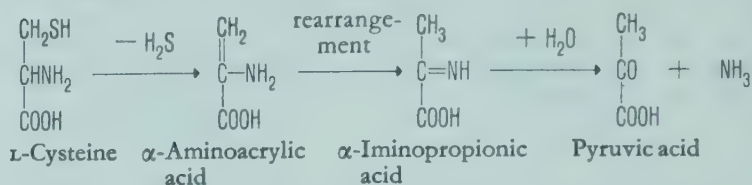
The ready interconversion of glycine and serine in animal tissues has been conclusively established. The cofactor requirement for the metabolism of "active" formaldehyde is complex¹³. It is possible that a major part of glycine shares the pathway of degradation with serine and thus yields acetyl-coenzyme A.

Another possible pathway of glycine degradation is initiated by the condensation with succinyl-coenzyme A^{14,15}:



The subsequent reactions up to the stage of δ -aminolevulinic acid have been firmly established¹⁶⁻¹⁷ but the pathway beyond δ -aminolevulinic acid leading eventually to succinyl coenzyme A is hypothetical and based on analogies.

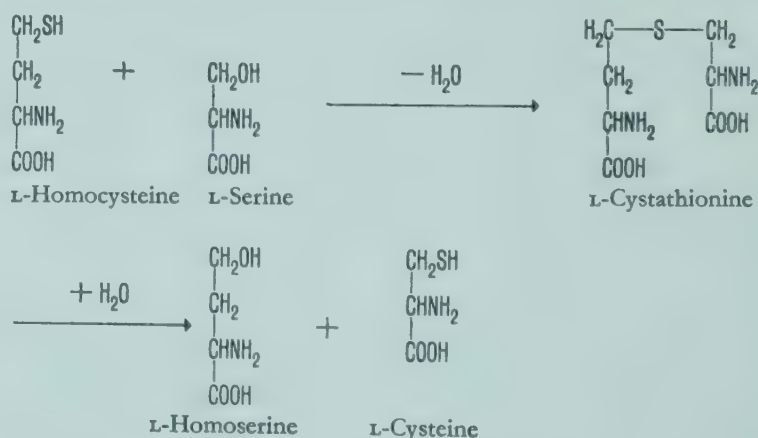
L-Cysteine can be desulfurated, under the influence of the enzyme desulfurase, to yield pyruvate, NH_3 and H_2S ^{18,19}. The intermediate stages have been formulated as follows:



These reactions are closely analogous to those of serine (see page 479).

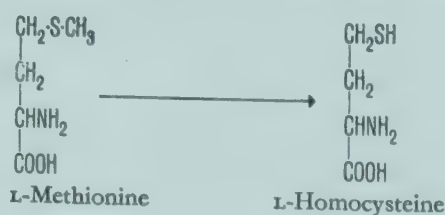
Cystine is converted in liver tissue into the same products as cysteine¹⁸; it is assumed that it undergoes reduction to cysteine before it is degraded.

L-Homocysteine also liberates H_2S in liver extracts, together with α -ketobutyrate and ammonia. There is no certainty about the intermediate stages. It is possible that desulfuration yields α -amino- α -vinylacetic acid, the fate of which is already described as a probable intermediate in the metabolism of homoserine (see above); it yields propionyl-coenzyme A. An alternative route is the transfer of the SH group to serine (transulfuration) with cystathionine an intermediate, in which case the end-product is likewise identical with that of homoserine:

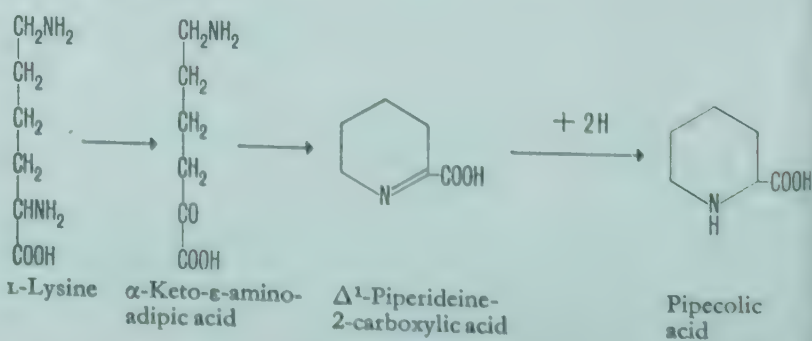


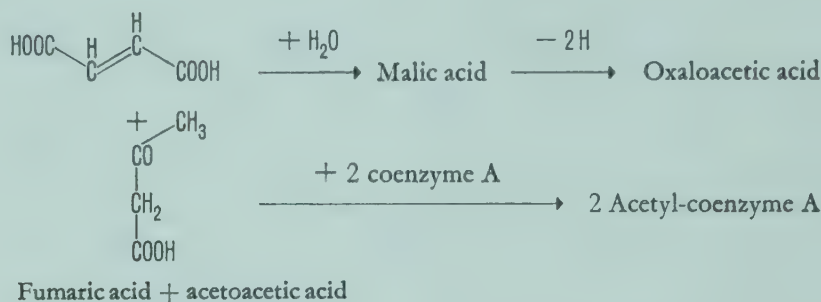
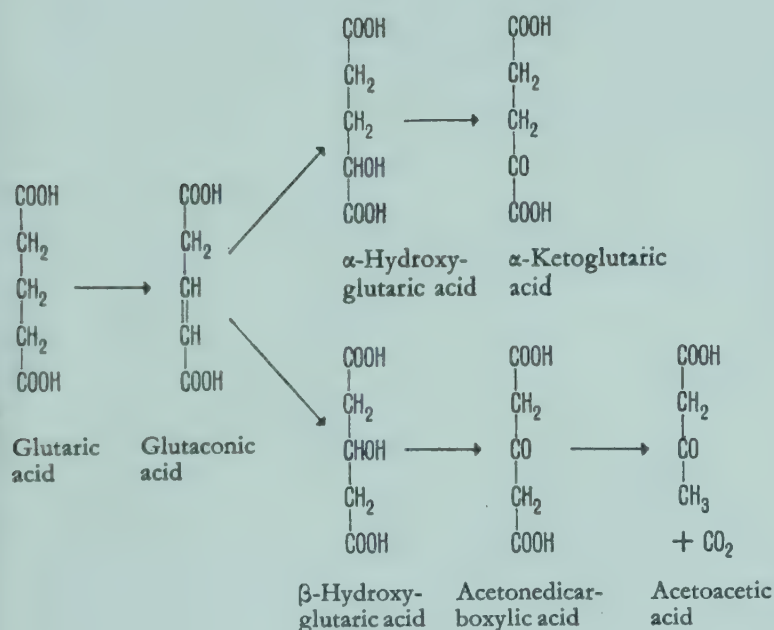
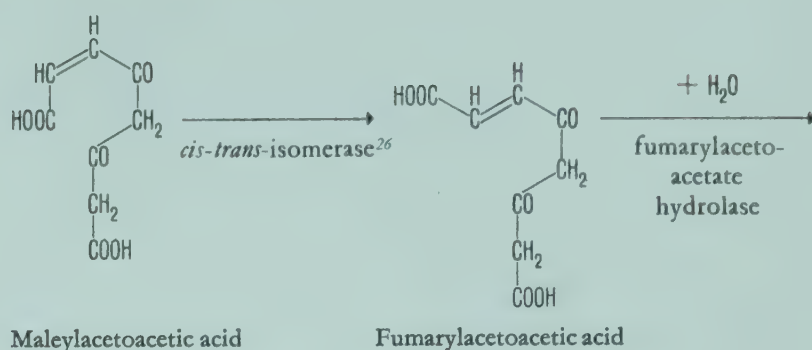
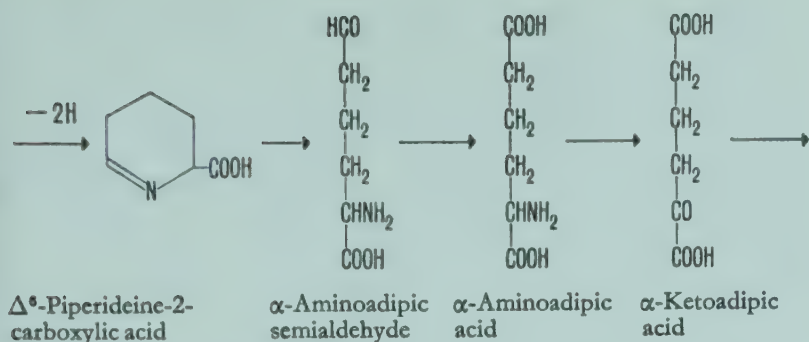
The evidence consists of the demonstration that homocysteine and serine form cystathionine in liver and that cystathionine, like homocysteine, is broken down to α -ketobutyrate and NH_3 ^{7,20}.

L-Methionine. The first stage in the degradation of L-methionine is the removal of the methyl group from the sulfur atom, which is effected by transfer to glycocyamine, ethanolamine, or other methyl acceptors. Demethylation results in the formation of homocysteine, the fate of which has already been discussed:



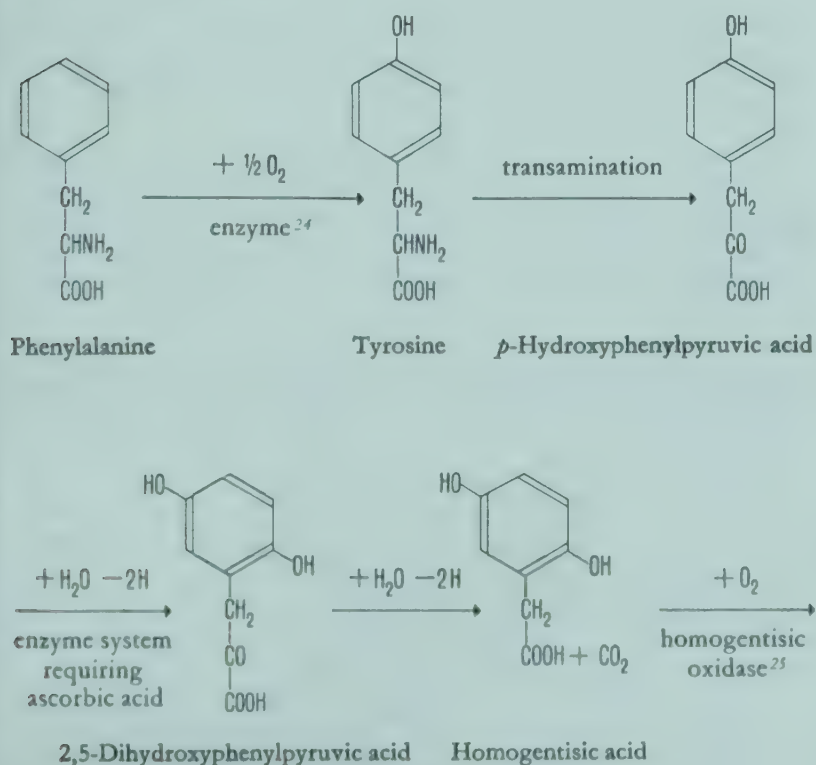
L-Lysine. The following pathway of the degradation of lysine is essentially based on isotopic evidence and the isolation of most of the intermediates^{21,22}:





Intermediates which have not been isolated are the two piperidinecarboxylic acids, glutaconic acid, β -hydroxyglutaric acid and acetonedicarboxylic acid. It is noteworthy that the ϵ -amino group of lysine becomes the α -amino group of aminoadipic acid. The end-products – α -ketoglutarate and acetoacetate (or acetate) – have been identified. The branching of the pathways resulting in two different products is assumed to occur at the stage of glutaconic acid. The formation of both α - and β -hydroxyglutarate from glutaconate is analogous to the action of aconitase. Aconitase does not control the manner in which H and OH are attached to the double bond of *cis*-aconitic acid²³, and two different hydroxy acids, *isocitric* and *citric* acid, are therefore formed. By analogy, glutaconic acid would yield α - and β -hydroxyglutaric acids on hydration.

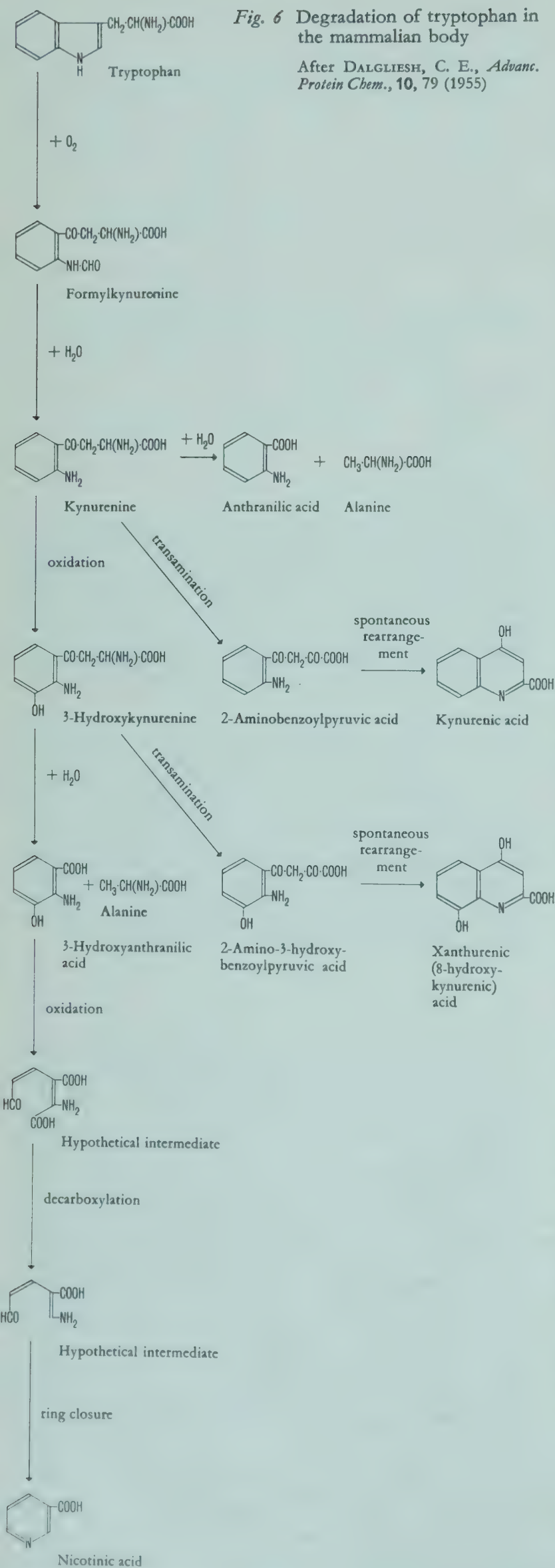
Phenylalanine and tyrosine are degraded in animal tissues by the reactions shown in the following scheme. Several unusual enzymes are involved. The end-products as formulated are oxaloacetic acid and acetyl-coenzyme A:



There are three types of inborn errors of metabolism where the disorder is due to insufficient formation (or nonformation) of one of the enzyme systems of the above sequence. In phenylketonuria the conversion of phenylalanine to tyrosine is blocked. As a consequence, phenylalanine undergoes an alternative degradation to phenylpyruvic acid, which accumulates since it is not readily broken down. In tyrosinosis the block is taken to be at the stage between *p*-hydroxyphenylpyruvate and 2,5-dihydroxyphenylpyruvate. In alkaptonuria, homogentisic oxidase is deficient.

Tryptophan is incompletely burned in man and in most animals. Products of incomplete oxidation which appear in the urine are anthranilic acid, kynurenine, hydroxykynurenine, kynurenic acid and 8-hydroxykynurenic ("xanthurenic") acid. Tryptophan and 3-hydroxyanthranilic acid (but not anthranilic acid) can be converted into nicotinic acid in some animals, though only in limited quantities. This involves a fission of the benzene ring of 3-hydroxyanthranilic acid and the formation of a pyridine ring, the nitrogen of which is derived from the amino group of anthranilic acid. The side chain of tryptophan can appear in the form of alanine. An outline of the probable pathways leading to the various products is given in Figure 6. Many details are still unknown.

- 1) For reviews see GREENBERG, D. M. (Ed.), *Chemical Pathways of Metabolism* vol. II, New York, 1954; McELROY and GLASS (Eds.), *A Symposium on Amino Acid Metabolism*, Baltimore, 1955; MEISTER, A., *Biochemistry of the Amino Acids*, New York, 1957.
- 2) STRECKER and MELA, *Biochim. biophys. Acta*, **17**, 580 (1955).
- 3) BACHHAWAT et al., *J. biol. Chem.*, **216**, 727 (1955); COON et al., in McELROY and GLASS (Eds.), *A Symposium on Amino Acid Metabolism*, Baltimore, 1955, page 431.
- 4) COON et al., *J. biol. Chem.*, **199**, 75 (1954); ROBINSON et al., *J. biol. Chem.*, **218**, 391 (1956).
- 5) COON et al., in McELROY and GLASS (Eds.), *A Symposium on Amino Acid Metabolism*, Baltimore, 1955, page 431; KINNORY et al., *J. biol. Chem.*, **212**, 385 (1955); ROBINSON et al., *J. biol. Chem.*, **224**, 1 (1957).
- 6) CHARGAFF and SPRINSON, *J. biol. Chem.*, **151**, 273 (1943).
- 7) CARROLL et al., *J. biol. Chem.*, **180**, 375 (1949).
- 8) MATSUO and GREENBERG, *J. biol. Chem.*, **215**, 547 (1955).
- 9) BINKLEY and OLSON, *J. biol. Chem.*, **185**, 881 (1950).
- 10) GREENBERG, D. M., *Chemical Pathways of Metabolism*, vol. II, New York, 1954, page 57.
- 11) BRAUNSHTEIN and VILENKINA, *C. R. Acad. Sci. U.S.S.R.*, **66**, 243 (1949).
- 12) MELTZER and SPRINSON, *J. biol. Chem.*, **197**, 461 (1952).
- 13) Cf. ARNSTEIN H. R. V., *Advanc. Protein Chem.*, **9**, 1 (1954); HUENNEKENS et al., *J. biol. Chem.*, **224**, 435 (1957).
- 14) SHERMAN and RUSSELL, *J. Amer. chem. Soc.*, **75**, 4873 (1953).
- 15) SHERMAN, D., *Harvey Lect.*, **50**, 258 (1954-55).
- 16) NEUBERGER and SCOTT, *Nature*, **172**, 1093 (1953).
- 17) RIMINGTON, C., *Brit. med. J.*, **2**, 189 (1956).
- 18) SMYTHE, C. V., *J. biol. Chem.*, **142**, 387 (1942).
- 19) FROMAGEOT, C., in SUMNER and MYRBACK (Eds.), *The Enzymes*, vol. I, part 2, New York, 1951, page 1237.
- 20) BINKLEY, F., *J. biol. Chem.*, **191**, 531 (1951).
- 21) BOROOK et al., *J. biol. Chem.*, **176**, 1383 (1948).
- 22) ROTHSTEIN and MILLER, *J. biol. Chem.*, **206**, 243 (1954); **211**, 851 and 859 (1954).
- 23) OGSTON, A. G., *Nature*, **167**, 693 (1951).
- 24) UDENFRIEND and MITOMA, in McELROY and GLASS (Eds.), *A Symposium on Amino Acid Metabolism*, Baltimore, 1955, page 876; MITOMA, C., *Arch. Biochem. Biophys.*, **60**, 476 (1956); KAUFMAN, S., *Biochim. biophys. Acta*, **23**, 445 (1957); KAUFMAN, S., *J. biol. Chem.*, **226**, 511 (1957).
- 25) SUDA and TAKEDA, *J. Biochem. (Tokyo)*, **37**, 381 (1950); CRANDALL, D. I., *J. biol. Chem.*, **212**, 565 (1955).
- 26) KNOX, W. E., in McELROY and GLASS (Eds.), *A Symposium on Amino Acid Metabolism*, Baltimore, 1955, page 836; KNOX and EDWARDS, *J. biol. Chem.*, **216**, 479, 489 (1955).

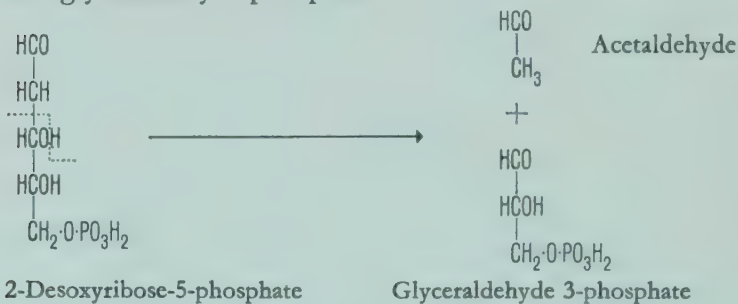


5. Degradation of food constituents other than carbohydrate, fat and protein

Foods contain a number of substances built up from molecules other than hexoses, fatty acids or amino acids. Some of these are not broken down in the body, but others are. To the latter group belong the constituents of nucleic acids and nucleotides (pentoses, deoxypentoses, purine bases, pyrimidine bases) and part of the cholesterol molecule. Quantitatively these substances form a very small part of the food and their contribution to the supply of energy is almost negligible.

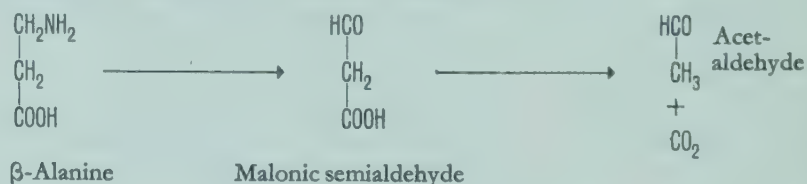
Pentoses, reacting in the form of ribose-5-phosphate, can be converted to glucose-6-phosphate and triose-phosphate by reactions of the pentose-phosphate cycle (reactions 3 to 8 of Table 19, page 501). Three molecules of ribose-5-phosphate form two molecules of glucose-6-phosphate and one molecule of glyceraldehyde phosphate.

2-Desoxyribose-5-phosphate can be split by aldolase to acetaldehyde and glyceraldehyde phosphate¹:



The acetaldehyde can be converted into acetyl-coenzyme A.

Purine bases are degraded in man to uric acid and in most mammals to allantoin (see page 483). *Pyrimidines* are broken down to ammonia, CO_2 and β -alanine or α -methyl- β -alanine (β -aminoisobutyric acid) by the reactions shown below. Both β -alanine and α -methyl- β -alanine can be further oxidized². β -Alanine can enter a transamination reaction with α -ketoglutarate to form the semialdehyde of malonic acid which is probably decarboxylated to acetaldehyde, a precursor of acetyl-coenzyme A³:



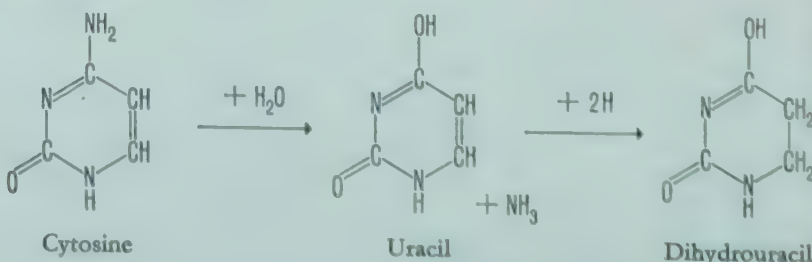
The analogous reactions of α -methyl- β -alanine would yield propionic aldehyde which is expected to form propionyl-coenzyme A and subsequently succinic acid.

About 5–10% of humans excrete α -methyl- β -alanine in the urine in quantities up to 300 mg daily⁴. This is assumed to be an inborn error of metabolism. It is probable that the defect is not due to the absence of enzymes responsible for the degradation but to a failure of tubular renal absorption⁵.

Of *cholesterol*, only the side chain undergoes complete oxidation. A specific enzyme can cleave off the side chain, forming isocaproic acid and leaving the ring system in the form of pregnenolone⁶. isocaproic acid in turn is broken down to propionic acid and acetyl-coenzyme A⁷. The ring system of cholesterol and steroids is not oxidized to CO_2 ⁸.

Other cell constituents which are essentially not oxidized in the body to CO_2 are the *iron porphyrins* derived from hemoglobin and cytochromes (these are excreted in the form of bile pigments and their derivatives), and the *uronic acids* contained in mucins, in hyaluronic acid and in the chondroitin sulfate of cartilage and tendons.

Degradation of pyrimidines. Cytosine and uracil are converted into β -alanine by the liver through the following reaction sequence. The evidence for these postulated reactions has not yet been fully investigated⁹.



(continued on page 484)

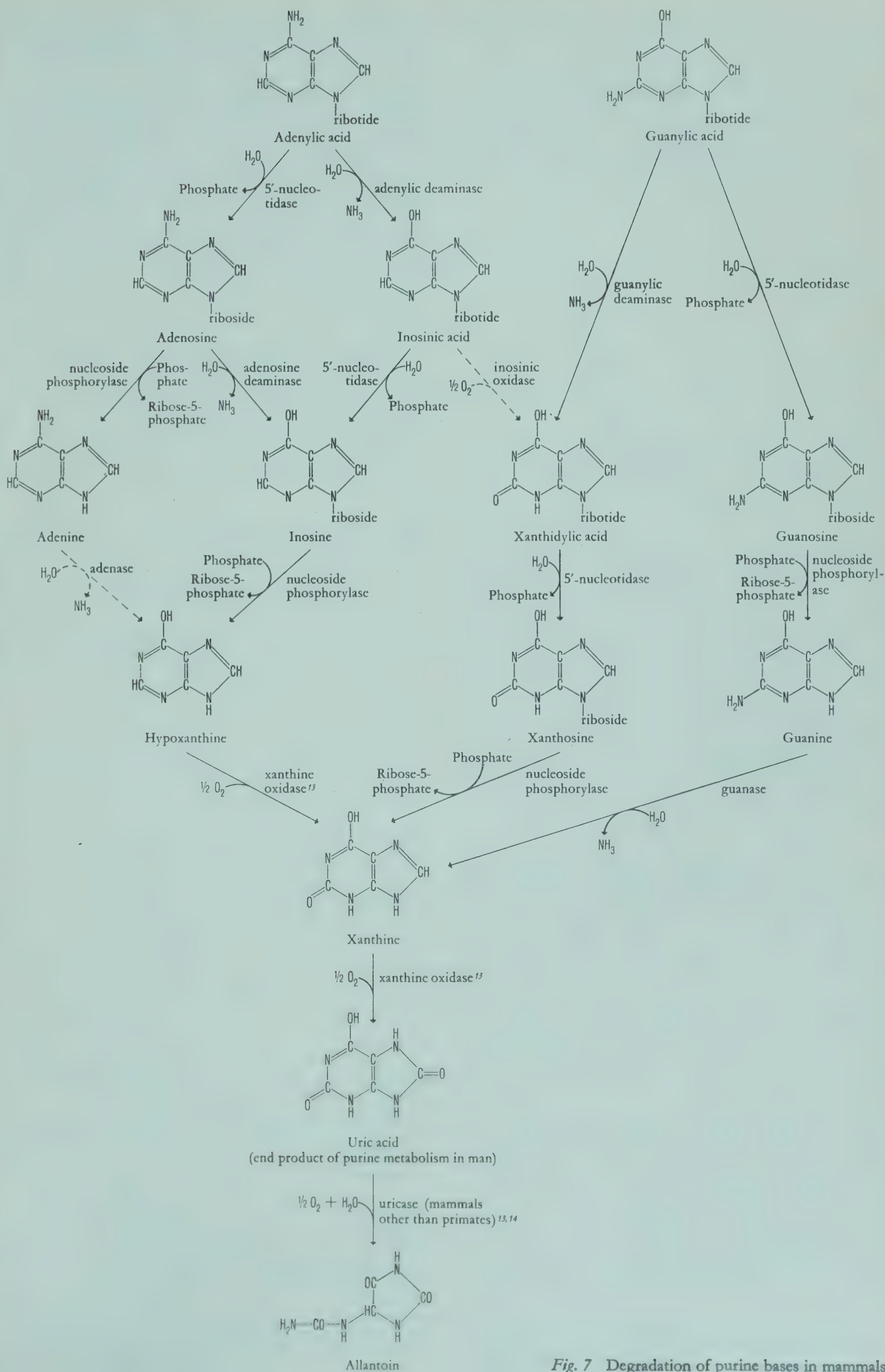
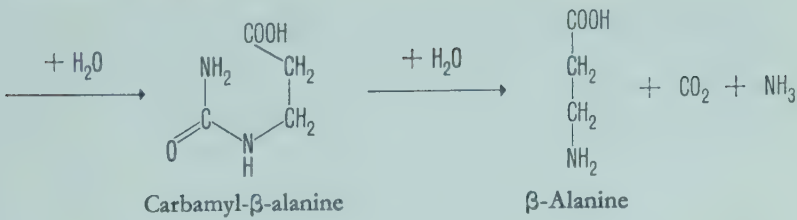


Fig. 7 Degradation of purine bases in mammals

(continued from page 482)



acetic acid in the form of acetyl-coenzyme A or an intermediate of the tricarboxylic acid cycle, α -ketoglutarate, succinate, fumarate or oxaloacetate. Acetic acid constitutes the main product: two-thirds of the carbon of carbohydrate and glycerol, all the carbon of the common fatty acids and about half the carbon skeleton of amino acids yield acetyl-coenzyme A. α -Ketoglutarate arises from glutamic acid, histidine, arginine, citrulline, ornithine, proline and hydroxyproline; oxaloacetate from aspartate; fumarate from part of the benzene ring of tyrosine and phenylalanine; succinate from isoleucine, valine, methionine, α -aminobutyric acid, propionic acid and the three terminal carbon atoms of fatty acids with an uneven number of carbon atoms.

The products of the first stage of the oxidative breakdown are completely oxidized in the second stage, the tricarboxylic acid cycle, which thus represents a common terminal pathway of oxidation shared by all foodstuffs. Almost two-thirds of the total energy released in the combustion of foodstuffs appears during the reactions of this cycle.

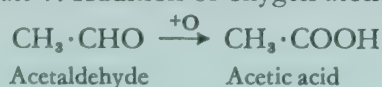
Any surplus oxaloacetate which is not required as a catalyst in the cycle can be decarboxylated to pyruvate, whence it is converted into acetyl-coenzyme A and undergoes complete oxidation.

In so far as substances other than carbohydrate, fat and amino acids can supply energy, their degradation follows pathways which, like those of carbohydrate, fat and amino acids, yield acetyl-coenzyme A and/or an intermediate of the tricarboxylic acid cycle.

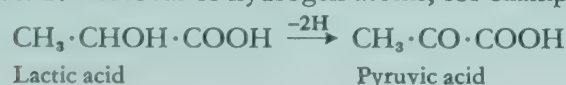
7. Mechanism of biological oxidations

General. The degradation reactions discussed so far take place when the foodstuff molecules are “burned” by molecular oxygen. This “combustion” is not, however, a direct reaction of molecular oxygen with the substrate but a transference of electrons, mediated by several complex enzyme systems, in which oxygen is the ultimate electron acceptor. In order to understand the action of these catalysts, it has to be borne in mind that biological oxidations include three types of reaction which at first sight appear to be different but which are basically the same. The three types are illustrated by the following cases:

Case 1. Addition of oxygen atoms, for example:



Case 2. Removal of hydrogen atoms, for example:

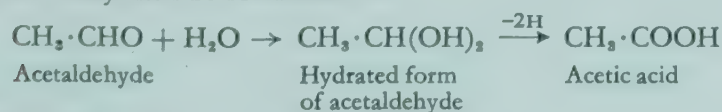


Case 3. Transformation of a metal from a lower to a higher valency state by removal of electrons, for example:

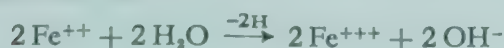


All three cases are seen to be basically similar – as removal of H atoms – if the participation of water is also considered:

Case 1 may then be formulated as



and **Case 3** as



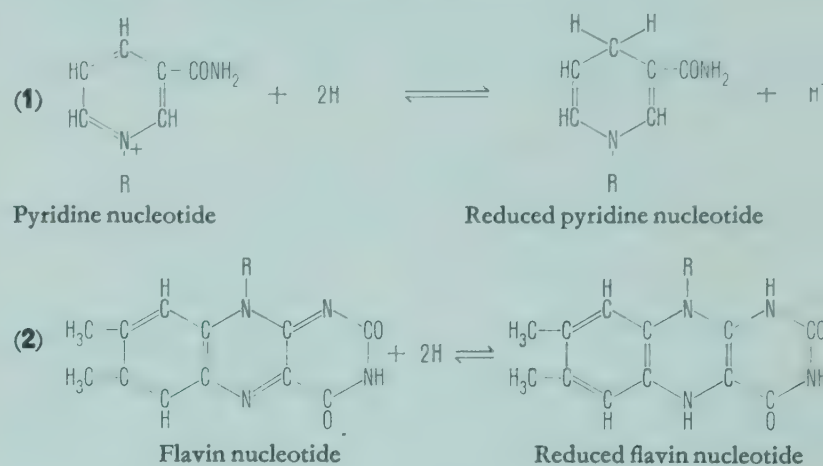
The common feature of all types of biological oxidations is a removal of electrons, although this is often either written as a removal of H (i.e. electron and proton) or as the addition of O atoms. There are instances in which neither H nor O atoms are directly involved, as in the oxidation of one heavy metal catalyst by another:



Such reactions occur in living cells between iron porphyrins (cytochromes) in which the electrons travel more or less directly from one Fe atom to another. Because there are cases where electron transfer is the only change, the formulation of oxidation as electron transport is looked upon as the most general and fundamental description of this process.

Biological oxidations may therefore be described in terms of the transfer of electrons, and the reactions whereby electrons are transferred from substrates to molecular oxygen are usually referred to as electron transport reactions.

The catalysts of biological oxidations¹. Three major types of catalysts participate in biological oxidations. They are enzymes which have as prosthetic groups respectively pyridine nucleotides, flavine nucleotides and iron porphyrins. The prosthetic groups undergo reversible oxidation and reduction. The catalysts thus exist in (at least) two forms, oxidized and reduced. The mechanism of reduction is illustrated by reaction (1) for a pyridine nucleotide, and by reaction (2) for a flavin nucleotide:



These reactions are written as similar to Case 2 above. The Fe atoms of iron porphyrin enzymes are reversibly oxidized and reduced as described in Case 3 above.

When mediating the reactions between substrate and molecular oxygen, i.e. when transferring electrons (or H atoms) from substrate to oxygen, these catalysts react in a characteristic order governed by their thermodynamic properties. These properties are indicated by the oxidation–reduction potentials of the catalysts:

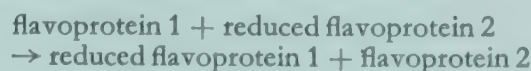
Catalyst	E'_0 (volts)
Oxygen electrode ($\text{H}_2\text{O} \rightleftharpoons \frac{1}{2}\text{O}_2 + 2\text{H} + 2e^-$)	+ 0.81
Cytochrome C	+ 0.25 ²
Flavin nucleotides (free)	– 0.20 ²
Pyridine nucleotides (free)	– 0.32 ²
Hydrogen electrode ($\text{H}_2 \rightleftharpoons 2\text{H}^+ + 2e^-$)	– 0.42

As seen from this table, the potentials of the electron carriers are such that the reduced form of pyridine nucleotides can act as reductant of the flavin nucleotides which, in turn, can act as reductant of the oxidized cytochromes. The order in which the catalysts transport electrons from the substrate to molecular oxygen may therefore be expressed in the following series of reactions:

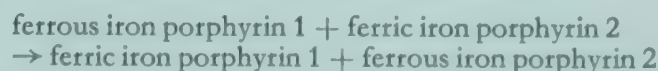
- (a) Substrate + pyridine nucleotide \rightarrow oxidized substrate + reduced pyridine nucleotide
- (b) Reduced pyridine nucleotide + flavin nucleotide \rightarrow pyridine nucleotide + reduced flavin nucleotide
- (c) Reduced flavin nucleotide + 2 Fe^{+++} -porphyrin \rightarrow flavin nucleotide + 2 Fe^{++} -porphyrin + 2 H^+
- (d) 2 Fe^{++} -porphyrin + 2 H^+ + $\frac{1}{2}\text{O}_2 \rightarrow$ 2 Fe^{+++} -porphyrin + H_2O



There are many variants of this basic scheme: firstly, because there are two pyridine nucleotides, many flavoproteins (some containing iron or molybdenum) and many iron porphyrins; secondly, because other types of reactions such as



or

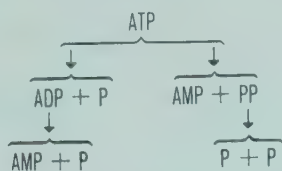


can be interspersed in the above series; thirdly, because additional catalysts may take part. There is evidence that both vitamin E and vitamin K are links in the hydrogen transport chain³.

1) For reviews see BALL, E. G., *Ann. N.Y. Acad. Sci.*, **45**, 363 (1944); HERBERT, D., *Ann. Rep. Progr. Chem.*, **47**, 335 (1951); SLATER, E. C., *Proceedings of the Third International Congress of Biochemistry, Brussels 1955*, New York, 1956, page 264; MAHLER and GREEN, *Science*, **120**, 7 (1954); MAHLER, H. R., *Proceedings of the Third International Congress of Biochemistry, Brussels 1955*, New York, 1956, page 252. 2) Values from BURTON, K., in KREBS and KORNBERG, *Ergebn. Physiol.*, **49**, 212 (1957). 3) MARTIUS, C., *Biochem. Z.*, **326**, 26 (1954); MARTIUS and NITZLITZOW, *Biochem. Z.*, **327**, 1 (1955); MARTIUS, C., *Proceedings of the Third International Congress of Biochemistry, Brussels 1955*, New York, 1956, page 1.

8. The key position of adenosine triphosphate (ATP) in biological energy transformations¹

One of the outstanding advances in the understanding of energy metabolism is the appreciation of the fact that the energy derived from the degradation of foodstuffs can be utilized for most purposes only if it is first transformed into a special type of chemical energy. This is the energy residing in the pyrophosphate bonds of adenosine triphosphate (ATP) which is released when these bonds are hydrolyzed to form inorganic orthophosphate (P) or pyrophosphate (PP), adenosine diphosphate (ADP) and adenosine monophosphate (adenylic acid, AMP):

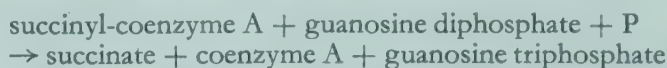


Pyrophosphate bonds release more free energy on hydrolysis (11–13 kcal according to conditions) than ester phosphate bonds (2–4 kcal). They are therefore referred to as “energy-rich”. It is the hydrolysis of the pyrophosphate bonds of ATP which provides the energy necessary for the various kinds of work performed by living cells, such as the contraction of muscle, the production of secretions, the activities of the nervous system and the synthesis of cell constituents.

The pyrophosphate bonds which are used up during the activities of the cells are resynthesized at the expense of the energy liberated by the degradation of foodstuffs. The synthesis of pyrophosphate bonds may in fact be looked upon as the first major object of the biological energy transformations. Special chemical mechanisms are required for the coupling between pyrophosphate bond synthesis and foodstuff degradation. It is evident that many hundreds of separate reactions occur when foodstuffs are degraded, but owing to the special arrangement of the metabolic processes coupling between degradation and pyrophosphate bond synthesis occurs only at a few stages. In all, six types of reaction are known in which energy becomes available for the synthesis of ATP. Two such stages occur in anaerobic glycolysis: when one molecule of glucose is converted into lactic acid two molecules of ATP are resynthesized from ADP and inorganic phosphate (Table 3, page 472). There are no more than four types of steps in the course of all the oxidative reactions where ATP is synthesized. The oxidative degradation of the substrate itself, i.e. the removal of two hydrogen atoms and their transfer to pyridine nucleotide, as a rule does not

supply energy. Energy is liberated when the hydrogen atoms or electrons are transferred from the pyridine nucleotides to molecular oxygen through the reactions 2, 3 and 4 discussed on page 485. Each of these three steps leads to the synthesis of one pyrophosphate bond (“oxidative phosphorylation”). The fourth step of the oxidative metabolism coupled with phosphorylation consists of reactions of type 1 (page 485) where the substrate is an α -ketonic acid. Reactions of this type where the substrate is not an α -ketonic acid do not yield appreciable amounts of energy and therefore cannot support the synthesis of pyrophosphate bonds.

The chemical mechanism by which the coupling between pyrophosphate synthesis and reactions 2, 3 and 4 is effected is unknown. Some information is available about the coupling mechanism between ATP synthesis and reactions of type 1 with α -ketonic acids as substrates. In this case an acyl-coenzyme A derivative is formed from the α -ketonic acid by the reactions described for pyruvate on page 474. Thus α -ketoglutarate yields succinyl-coenzyme A. The latter reacts as follows:



Phosphoryl succinate or phosphoryl-coenzyme A may be intermediates in this reaction though neither has as yet been identified². Guanosine triphosphate can transfer phosphate to ADP:



Adenosine triphosphate contains two “energy-rich” pyrophosphate bonds. It is probable that only the terminal bond serves as an immediate source of energy, or can be directly resynthesized. The second pyrophosphate bond is used to re-phosphorylate adenosine diphosphate according to the reaction



which is catalyzed by the enzyme adenylate kinase (also called myokinase) present in all tissues. The balance of this reaction plus the hydrolysis of ATP to ADP + P represents an hydrolysis of ADP to AMP + P. In reverse the reaction represents a mechanism for the re-phosphorylation of AMP.

1) For references see KREBS and KORNBERG, *Ergebn. Physiol.*, **49**, 212 (1957).
2) SANADI et al., *Biochim. biophys. Acta*, **13**, 146 (1954); **14**, 434 (1954); KAUFMAN, S., *J. biol. Chem.*, **216**, 153 (1955); COHN, M., *Biochim. biophys. Acta*, **20**, 92 (1956).

Digestive enzymes

In this section will be described the specific enzymes the combined action of which is responsible for the process of digestion of foodstuffs. Each enzyme catalyzes the hydrolysis of one compound or of a series of closely related compounds. (For a general review of enzymes and enzyme action see pages 467–469.)

1. Proteolytic enzymes (proteases)

These are enzymes which catalyze the hydrolytic cleavage of peptide bonds:



They may be divided into two main classes:

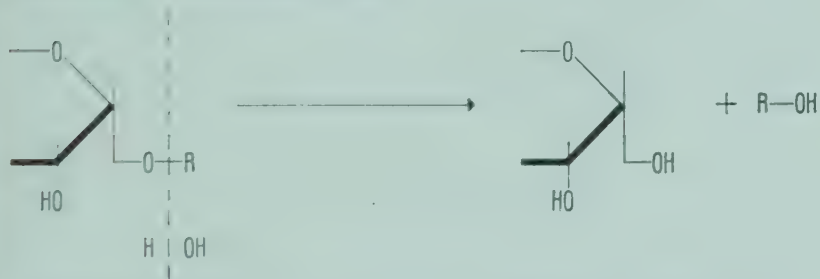
1. *Endopeptidases*, which act on proteins and peptides by hydrolyzing "internal" peptide linkages, i.e. those situated away from the ends of peptide chains.

2. *Exopeptidases*, which catalyze the hydrolysis of peptide bonds situated at the ends of peptide chains. These enzymes are specific for peptides possessing one or more free terminal α -amino or α -carboxyl groups.

Members of both classes of proteases are widely distributed in mammalian tissues. Those of the gastrointestinal tract are discussed in Tables 10 and 11, pages 488–491. The proteases of other tissues are summarized in Table 12 (pages 491–492).

2. Glycosidases

Carbohydrates are digested by these enzymes, which catalyze the hydrolysis of glycosidic bonds:



Some glycosidases act on only the glycosidic bonds of polysaccharides (polysaccharidases), others on only those of smaller carbohydrates (oligosaccharidases). A number of factors determine whether a glycosidase will act on any particular linkage. Among these factors the most important are

(a) the nature of the monosaccharide which donates the reducing group involved in the glycosidic bond; for example, separate enzymes act on glucosides and galactosides;

(b) the configuration (α or β) about the carbon atom of the potential reducing group:



(c) the configuration (D- or L-) of the monosaccharide bearing the potential reducing group. In general, mammalian glycosidases act only at linkages of the D-configuration;

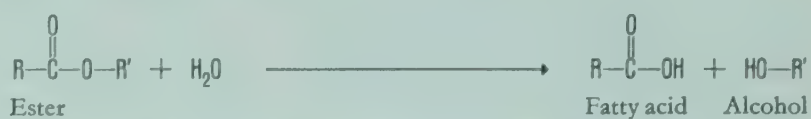
(d) the size of the heterocyclic sugar ring. Usually, glycosidases which act on aldohexosides are specific for linkages in which the aldohexose is in the pyranose form, whilst those acting on ketohexosides require the substrate to be in the furanose form:



The general properties of mammalian glycosidases are described in Table 13 (pages 493–494).

3. Lipases and esterases

Fats and other esters are hydrolyzed by the action of enzymes which have been subdivided into *lipases*, which hydrolyze the ester linkages between both short-chain and long-chain fatty acids and glycerol, and thus act on fats, and *esterases*, which act only slowly on fats but split the ester linkages between other acids and other alcohols. The general action of this group of enzymes may be formulated as follows:



The lipases of the gastrointestinal tract are discussed in Table 14 (page 494). Other lipases such as those of serum, leukocytes, erythrocytes, cerebrospinal fluid, milk, pleural effusions, lymph, liver, lung, brain, muscle, skin, testes, etc., behave similarly; like those of the gastrointestinal tract, they hydrolyze fats and short-chain fatty acid esters¹.

Phosphatases

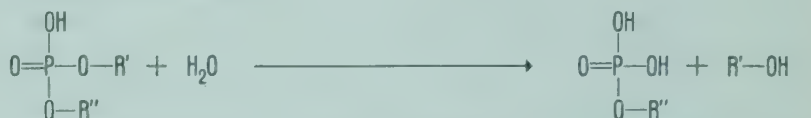
Mammalian tissues contain a variety of unspecific esterases which have not yet been obtained in a pure form. Some of these enzymes catalyze the hydrolysis of the ester linkages between short-chain fatty acids and alcohol, others hydrolyze esters of the type $\text{R} \cdot \text{OR}'$, where R is not a carboxylic acid. The largest group of these enzymes is formed by the *phosphatases*². These may be further classified as:

1. *Phosphomonoesterases*, which hydrolyze monoesters of phosphoric acid:

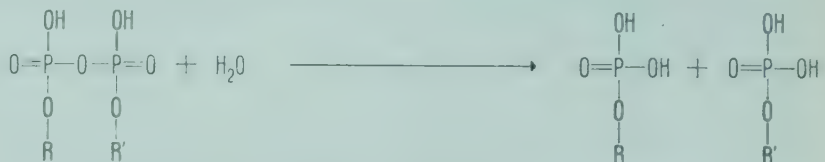


For example, glucose-6-phosphate is hydrolyzed to glucose and phosphate.

2. *Phosphodiesterases*, which hydrolyze substrates such as nucleic acids, or the synthetic substrate diphenyl orthophosphate, at one of the ester linkages:



3. *Pyrophosphatases*, which hydrolyze the pyrophosphate linkages of salts of pyrophosphoric acid and of pyrophosphate esters:



4. *Metaphosphatases*, which hydrate metaphosphates to orthophosphates:



These have not been demonstrated to occur in the mammalian body.

Sulfatases³

These enzymes catalyze the hydrolysis of esters of sulfuric acid:



They may be distinguished according to the nature of the sulfuric acid esters which they hydrolyze.

The esterases in general are listed in Table 15 (pages 495–496); those acting on phospholipids and their metabolic products are further discussed in Table 16 (pages 496–497).

4. Ribonucleases and deoxyribonucleases

Ribonucleases (RNAases) and deoxyribonucleases (DNAases) catalyze the cleavage of ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) respectively (Table 17, pages 497–498). They are present in most if not all tissues⁴.

Of the RNAases only pancreatic RNAase has been studied extensively. The enzyme is a specific phosphodiesterase which hydrolyzes certain phosphoric ester linkages of RNA but not of DNA. The end-products of the prolonged action of pancreatic RNAase are 3'-uridylic acid, 3'-cytidylic acid, and a large number of

Table 10 Proteases and protease precursors of the gastrointestinal tract (continued) (For references see end of table, page 490)

Enzyme	Location	Approx. mol. wt.	Optimal pH of action	Reaction catalyzed*	Remarks
Trypsinogen	Pancreas	23,700 ⁶	—	—	Nonenzymic precursor of trypsin, into which it is converted by enterokinase and, autocatalytically, by trypsin. During this conversion, a fragment of probable structure valine-(aspartate) ₄ -lysine is split off from the N-terminal end of trypsinogen by the scission of a lysyl-isoleucyl bond ⁶
Enterokinase	Small intestine	—	ca. 6	Converts trypsinogen to trypsin + a small fragment + some inert protein	The formation of the inert protein is suppressed by Ca ⁺⁺ ; the relative amount formed is dependent on the pH ⁷
Trypsin	Small intestine	23,800	7 – 8	$\begin{array}{c} \text{R} \\ \\ -\text{CO}-\text{NH}-\text{CH}-\text{CO}-\text{X} \\ \\ \text{---} \end{array}$ <p>where R = δ-guanidino-<i>n</i>-propyl or ϵ-amino-<i>n</i>-butyl (from L-arginine or L-lysine). Can also hydrolyze esters of arginine or lysine⁸</p>	Can act on many types of protein, but acts more rapidly on denatured than on native proteins. Does not clot milk, but decreases the clotting time of blood. Activity enhanced by Ca ⁺⁺
α -Chymotrypsinogen	Pancreas	22,500	—	—	Nonenzymic precursor of the chymotrypsins, to which it is converted by trypsin and, autocatalytically, by chymotrypsins. It is believed ⁹ that the conversion of α -chymotrypsinogen to δ -chymotrypsin involves the successive action of trypsin and chymotrypsin on the peptide sequence [-leucine-serine-arginine-isoleucine-] within the cyclic α -chymotrypsinogen molecules. Trypsin attacks the arginyl-isoleucyl bond to form π -chymotrypsin; this is followed by autolysis of the leucyl-seryl bond to yield δ -chymotrypsin. Serylarginine is formed in this reaction. Autolytic cleavage of a tyrosyl-alanyl bond of δ -chymotrypsin then yields α -chymotrypsin, which is the enzyme normally predominant in the pancreatic juice
Chymotrypsinogen B	Pancreas	22,500	—	—	Yields chymotrypsin B on activation by trypsin. Differs from α -chymotrypsinogen in electrophoretic mobility and in the ease with which it is retained on resins ¹⁰
Chymotrypsins: π	Pancreas	—	—	Similar in action to α -chymotrypsin	First product of tryptic digestion of α -chymotrypsinogen. Very unstable: obtained only at low temperature. Rapidly converted to δ - and α -chymotrypsins. 2–2½ times as active as α -chymotrypsin
δ	Pancreas	—	—	Similar in action to α -chymotrypsin	Derived from π -chymotrypsin, with loss of serylarginine. Unstable. Approximately 1½ times as active as α -chymotrypsin

* These specificity relationships are those elucidated by the action of the enzymes on synthetic peptides; they are not necessarily those of the enzymes acting on proteins¹.

Table 10 Proteases and protease precursors of the gastrointestinal tract (concluded)

Enzyme	Location	Approx. mol. wt.	Optimal pH of action	Reaction catalyzed*	Remarks
Chymotrypsins (continued): α	Pancreas	21,500	ca. 8	<div>$\begin{array}{c} \text{R} \qquad \qquad \text{R}' \\ \qquad \qquad \\ -\text{CO}-\text{CH}-\text{NH}-\text{CO}-\text{CH}-\text{NH}- \\ \qquad \qquad \\ \text{---} \qquad \text{---} \end{array}$<p>where R' = <i>p</i>-hydroxyphenyl from tyrosine. If the group R'·CH(NH)·CO- is a phenylalanine, tryptophan or methionine residue, decreased activity persists. Rupture of C–C bonds has also been reported¹¹</p></div>	Predominant chymotrypsin in the pancreatic secretion. Unlike trypsin, it clots milk but not blood
β	Pancreas	30,000 (probably as a dimer)	ca. 8	Similar in action to α-chymotrypsin	Produced by limited autolysis of α-chymotrypsin. Differs from α-chymotrypsin in crystalline form, solubility and rate of inactivation by acids, alkalis and urea ¹²
γ	Pancreas	27,000 (probably as a dimer)	ca. 8	Similar in action to α-chymotrypsin	Probably a product of the further autolysis of β-chymotrypsin
B	Pancreas	22,500	ca. 8	Similar in action to α-chymotrypsin	Differs from the α-enzyme in crystalline form and electrophoretic mobility. Has lower activity towards casein than α-chymotrypsin

* These specificity relationships are those elucidated by the action of the enzymes on synthetic peptides; they are not necessarily those of the enzymes acting on proteins¹.

1) See BERGMANN, M., *Advanc. Enzymol.*, **2**, 49 (1942); FRUTON, J. S., *Ann. Rev. Biochem.*, **16**, 35 (1947). 2) HERRIOTT, R. M., *J. gen. Physiol.*, **24**, 325 (1940-41). 3) MASCH and HUCHTING, *Hoppe-Seyl. Z. physiol. Chem.*, **301**, 49 (1955). 4) HOLTER and LI, *Acta chem. scand.*, **4**, 1321 (1950); MATTENHEIMER et al., *Helv. chim. Acta*, **35**, 1970 (1952). 5) TIETZE, F., *J. biol. Chem.*, **204**, 1 (1953). 6) DAVIE and NEURATH, *J. biol. Chem.*, **212**, 515 (1955); DESNUELLE and FABRE, *Biochim. biophys. Acta*, **18**, 49 (1955). 7) McDONALD and KUNITZ, *J. gen. Physiol.*, **25**, 53 (1941-42). 8) NEURATH and SCHWERT, *Chem. Rev.*, **46**, 69 (1950). 9) FRUTON and MYCEK, *Ann. Rev. Biochem.*, **25**, 57 (1956). 10) LASKOWSKI, M., in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. II, New York, 1955, page 8. 11) DOHERTY, D. G., *J. Amer. chem. Soc.*, **77**, 4887 (1955). 12) SMITH, E. L., in SUMNER and MYRBÄCK (Eds.), *The Enzymes*, vol. I, part 2, New York, 1951, page 793.

Table 11 Exopeptidases and exopeptidase precursors of the gastrointestinal tract¹ (For references see end of table, page 491)

A large number of different exopeptidases have been recognized as occurring in the gastrointestinal tract. They are distinguished from each other mainly in their specificities of action on synthetic peptides. Only a few have been purified extensively, and the list of exopeptidases here given is not complete: doubtless many more remain to be isolated and studied

Enzyme	Location	Approx. mol. wt.	Optimal pH of action	Reaction catalyzed*	Remarks
Procarboxypeptidase	Pancreas	96,000	—	—	Nonenzymic precursor of carboxypeptidase. Is more acidic than carboxypeptidase, and is split by trypsin to carboxypeptidase and fragments. All the potential carboxypeptidase activity of procarboxypeptidase is retained in the smaller carboxypeptidase fragment: the larger fragment is enzymically inactive ²
Carboxypeptidase	Pancreas	34,000 ³⁻⁴	7.5 – 8.5	<div>$\begin{array}{c} \text{R}' \\ \\ \text{R}-\text{CO}-\text{NH}-\text{CH}-\text{COOH} \\ \\ \text{---} \end{array}$<p>Wide specificity, but most active when R' = benzyl from phenylalanine. Also acts when R' is derived from tyrosine > tryptophan > leucine > methionine > isoleucine > alanine > glycine. Also acts on esters. Terminal carboxyl must be free; may also require the presence of uncharged amino groups</p></div>	Contains Zn ⁺⁺ as essential constituent ⁴ . Strongly inhibited by sulfide, cyanide, iodoacetate; sulfhydryl groups in the protein necessary for activity. Also inhibited by aromatic D-amino acids, by aromatic and heterocyclic carboxylic acids and, most effectively, by β-phenylpropionic acid

* These specificity relationships are those elucidated by the action of the enzymes on synthetic peptides; they are not necessarily those of the enzymes acting on proteins².

Table 11 Exopeptidases and exopeptidase precursors of the gastrointestinal tract¹ (continued)

Enzyme	Location	Approx. mol. wt.	Optimal pH of action	Reaction catalyzed*	Remarks
Amino-tripeptidase (tripeptidase)	Small intestine ⁵	–	7.5 – 8.5	$\begin{array}{c} \text{R} \qquad \qquad \text{R}' \qquad \qquad \text{R}'' \\ \qquad \qquad \qquad \qquad \\ \text{H}_2\text{N}-\text{CH}-\text{CO}-\text{NH}-\text{CH}-\text{CO}-\text{NH}-\text{CH}-\text{COOH} \\ \\ \text{Hydrolyzes a wide variety of tripeptides. Requires free amino group} \end{array}$	Hydrolyzes tripeptides at the bond adjacent to the essential free amino group to yield a free amino acid and a dipeptide. Has little or no action on tetra- or dipeptides
L-Leucine amino-dipeptidase	Small intestine	–	Prob. ca. 8	$\begin{array}{c} \text{R} \qquad \qquad \text{R}' \\ \qquad \qquad \\ \text{H}_2\text{N}-\text{CH}-\text{CO}-\text{NH}-\text{CH}-\text{COOH} \\ \\ \text{Wide specificity, but most active when R = L-leucine residue. Also attacks polypeptides, but more slowly} \end{array}$	Activated by Mg ⁺⁺ or Mn ⁺⁺ , inhibited by anions which will bind Mg ⁺⁺ or Mn ⁺⁺ , e.g. citrate, ethylenediamine tetraacetate, pyrophosphate. Not affected by reagents reacting with sulfhydryl groups
Glycylglycine dipeptidase ⁶	Small intestine	–	ca. 8	$\begin{array}{c} \text{R} \qquad \qquad \text{R}' \\ \qquad \qquad \\ \text{H}_2\text{N}-\text{CH}-\text{CO}-\text{NH}-\text{CH}-\text{COOH} \\ \\ \text{where R = glycine or sarcosine residue, R' = glycine residue} \end{array}$	Probably a metal enzyme: contains Co ⁺⁺ as essential constituent. It has been postulated that Co ⁺⁺ acts as a bridge in forming chelate complexes between the enzyme and its substrate
Glycyl-L-leucine dipeptidase ⁷	Small intestine	–	ca. 8	Optimally specific for L-leucine. Also hydrolyzes sarcosyl-L-leucine	Activated by Mn ⁺⁺
Imido-dipeptidase (prolidase)	Small intestine	–	ca. 8	$\begin{array}{c} \text{R} \qquad \qquad \text{[OH]} \\ \qquad \qquad \\ \text{H}_2\text{N}-\text{CH}-\text{CO}-\text{N} \begin{array}{c} \diagup \diagdown \\ \text{COOH} \end{array} \\ \text{or} \\ \text{H}_2\text{N}-\text{CH}-\text{CO}-\text{N}-\text{CH}_2-\text{COOH} \\ \\ \text{CH}_3 \end{array}$	Hydrolyzes only dipeptides lacking a peptide hydrogen. Activated by Mn ⁺⁺ . Inhibited strongly by iodoacetamide and p-chloromercuribenzoate in the absence of, but not in the presence of, Mn ⁺⁺ : this suggests that Mn ⁺⁺ is bound to a sulfhydryl group of the protein ⁸
Imino-dipeptidase (prolinase)	Small intestine	–	ca. 8	$\begin{array}{c} \text{[HO]} \\ \\ \text{N} \begin{array}{c} \diagup \diagdown \\ \text{CO} \end{array} - \text{NH}-\text{CH}-\text{COOH} \\ \\ \text{where R = any amino acid residue except glutamic or aspartic acid} \end{array}$	Hydrolyzes dipeptides containing N-terminal proline or hydroxyproline residues. Activated by Mn ⁺⁺

* These specificity relationship are those elucidated by the action of the enzymes on synthetic peptides; they are not necessarily those of the enzymes acting on proteins².

1) For a review see SMITH, E. L., in SUMNER and MYRBÄCK (Eds.), *The Enzymes*, vol. I, part 2, New York, 1951, page 793. 2) BERGMANN, M., *Advanc. Enzymol.*, **2**, 49 (1942); FRUTON, J. S., *Ann. Rev. Biochem.*, **16**, 35 (1947). 3) SMITH et al., *J. biol. Chem.*, **180**, 33 (1949). 4) VALLEE and NEURATH, *J. Amer. chem. Soc.*, **76**, 5006 (1954). 5) ÅGREN, G., *Acta physiol. scand.*, **9**, 248, 255, 269 (1945). 6) SMITH, E. L., in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. II, New York, 1955, page 107. 7) SMITH, E. L., in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. II, New York, 1955, page 105. 8) SMITH et al., in MCELROY and GLASS (Eds.), *The Mechanism of Enzyme Action*, Baltimore, 1954, page 291.

Table 12 Proteases of tissues other than the gastrointestinal tract (For references see end of table, page 492)

It has long been known that animal tissues other than the gastrointestinal tract contain proteolytic enzymes since, on the death of animals, extensive breakdown of tissue proteins occurs. The tissue proteinases are now referred to as cathepsins: they occur in most tissues, the liver, spleen and kidney being particularly rich in them. In addition to these proteinases, which have been only partially purified, tissues contain exopeptidases analogous to, or identical with, those of the gastrointestinal tract. The list of endo- and exo-peptidases here given cites only those enzymes which up to the present have been well characterized. The proteases of blood-clotting, and the proteases acting on dehydropeptides and acylpeptides (acylase I and II) are also not discussed here

Enzyme	Location	Optimal pH of action	Reaction catalyzed*	Remarks
Cathepsin A	Most animal tissues, particularly liver, spleen and kidney. The skin, uterus, lung, muscles and brain are poor in activity ¹	5.6	Similar in action to pepsin	Old name: cathepsin I. Requires no activator
Cathepsin B		ca. 5	Similar in action to trypsin	Old name: cathepsin II. Activated by compounds containing sulfhydryl groups

* These specificity relationships have been elucidated by the use of synthetic substrates; they are not necessarily those of the enzymes acting on proteins².

Table 12 Proteases of tissues other than the gastrointestinal tract (continued)

Enzyme	Location	Optimal pH of action	Reaction catalyzed*	Remarks
Cathepsin C	Most animal tissues, particularly liver, spleen and kidney. The skin, uterus, lung, muscles and brain are poor in activity ¹	ca. 5 for proteolysis; ca. 7 for transamidation	Similar in action to chymotrypsins	Activated by compounds containing sulfhydryl groups. At pH 7 acts as transamidase: when acting on a peptide amide, the NH ₂ group split off by water can be transferred not only to the H ⁺ of water (in which case a normal hydrolytic reaction occurs and ammonia is formed) but also to other NH ₂ acceptors, such as H of another NH ₂ group. Thus, with glycyl-L-phenylalanineamide NH ₂ ·CH ₂ ·CO·NH·CH(CH ₂ ·C ₆ H ₅)·CO·NH ₂ successive transamidations occur, ² leading to the formation of insoluble polypeptides: NH ₂ ·R·CO·NH ₂ + NH ₂ ·R·CO·NH ₂ → NH ₂ ·R·CO·NH·R·CO·NH ₂ + NH ₃
Carboxypeptidase	Most animal tissues	ca. 7	Homospecific with pancreatic carboxypeptidase	Old name: cathepsin IV
Amino-tripeptidase (tripeptidase)	Most animal tissues; has been purified from calf thymus ³ and from equine erythrocytes ⁴	8.0	Similar in action to intestinal tripeptidase	Inhibited by cysteine, Cd ⁺⁺ , Hg ⁺⁺ . Rapidly inactivated in acid media
L-Leucine amino-dipeptidase	Many tissues; especially abundant in kidney	8 – 9	Similar in action to the intestinal enzyme	Old name: cathepsin III. The enzyme protein, isolated from swine kidney, ⁵ is particularly rich in leucine (8.8%). Requires activation by Mg ⁺⁺ or Mn ⁺⁺
Glycylglycine dipeptidase	Many tissues; has been partially purified from rat muscle, human uterus and swine kidney ⁶	7.6	Similar in action to the intestinal enzyme	Activity enhanced by addition of Co ⁺⁺ or, more weakly, of Mn ⁺⁺ . Preparations of this enzyme from rat muscle are exceedingly unstable, from human uterus less so ⁶
Glycyl-L-leucine dipeptidase	Several tissues; has been partially purified from uterus ⁶	ca. 8	Similar in action to the intestinal enzyme	Activity enhanced by Zn ⁺⁺ and phosphate
Imido-dipeptidase (prolidase)	Many tissues; has been found in skeletal and smooth muscle, erythrocytes, serum, pituitary, lung and kidney, and has been partially purified from equine erythrocytes and swine kidney ⁶	7.8 – 8.0	Similar in action to the intestinal enzyme	Activity enhanced by Mn ⁺⁺
Imino-dipeptidase (prolinase)	Many tissues; has been partially purified from swine kidney ⁶	ca. 8	Similar in action to the intestinal enzyme	Activity enhanced by Mn ⁺⁺ and Cd ⁺⁺
Carnosinase	Several tissues; has been partially purified from spleen, liver and swine kidney ⁶	8.0 – 8.4 in presence of Mn ⁺⁺ , 7.8 – 7.9 in presence of Zn ⁺⁺ , 7.4–7.5 in absence of metal	A dipeptidase, hydrolyzing L-alanyl-L-histidine > glycyl-L-histidine > β-alanyl-L-histidine > D-alanyl-L-histidine	Activity enhanced by Zn ⁺⁺ and Mn ⁺⁺

* These specificity relationships have been elucidated by the use of synthetic substrates: they are not necessarily those of the enzymes acting on proteins⁷.
1) SMITH, E. L., in SUMNER and MYRBÄCK (Eds.), *The Enzymes*, vol. I, part 2, New York, 1951, page 793. 2) DE LA HABA et al., in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. II, New York, 1955,

page 64. 3) ELLIS and FRUTON, *J. biol. Chem.*, **191**, 153 (1951). 4) ADAMS et al., *J. biol. Chem.*, **199**, 845 (1952). 5) SPACKMAN et al., *J. biol. Chem.*, **212**, 255 (1955). 6) SMITH, E. L., in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. II, New York, 1955, page 93. 7) BERGMANN, M., *Advanc. Enzymol.*, **2**, 49 (1942); FRUTON, J. S., *Ann. Rev. Biochem.*, **16**, 35 (1947).

Table 13 Glycosidases (For references see end of table, page 494)

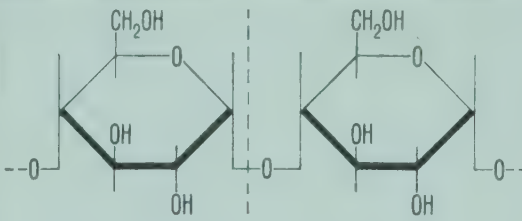
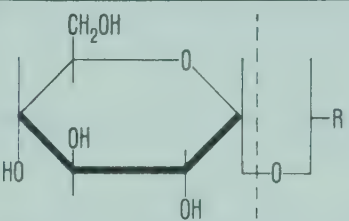
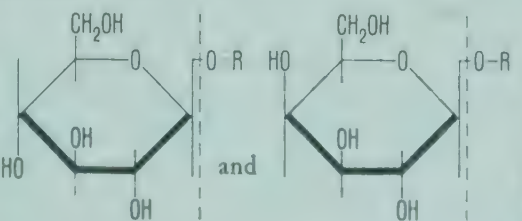
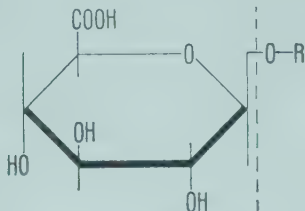
Enzyme	Location	Optimal pH of action	Reaction catalyzed	Remarks
α -Amylase	Saliva, pancreatic juice, blood	6.9		Hydrolyzes α -1,4-glucosidic bonds in polyglucosans such as amylose, amylopectin, glycogen and dextrins. The initial stage of action of the enzyme is characterized by a rapid decrease of the mol.wt. of the substrate, resulting in a rapid change of its iodine-staining properties; when starch paste is the substrate, a rapid decrease of viscosity (liquefaction) occurs. The enzyme preferentially attacks the second linkage from the reducing end of the polyglucosan molecule, producing maltose, dextrins and a small amount of glucose ¹ . Activity of the enzyme is enhanced by $\text{Cl}^- > \text{Br}^- > \text{NO}_3^- > \text{I}^-$. Human salivary and pancreatic α -amylases are identical ²
Maltase	Small intestine, pancreatic juice, blood, liver ³	6.6	 where R = glucose (in which case the above compound is maltose, 4- α -D-glucopyranosyl-D-glucose), substituted hexoses, phenols, terpenes, etc. ⁴ . The evidence for the rupture of the glucose-O bond rests on isotopic data ⁵	An α -glucosidase: the maltose produced from the digestion of starch by α -amylase is hydrolyzed to glucose by this enzyme. Inhibited by the glucose formed. Does not act on sucrose. Claims for the existence of an animal sucrase, and its suggested identity with maltase, have been disputed ^{4,6}
Oligo-1,6-glucosidase	Small intestine	ca. 7	Hydrolyzes 1,6-glucoside linkages of <i>iso</i> -maltose, panose, and α -amylase dextrins ⁷	This enzyme is thought to complete the digestion of starch by hydrolyzing the dextrins produced by α -amylase to smaller unbranched molecules, which can be further degraded by α -amylase and maltase in the pancreatic juice
Amylo-1,6-glucosidase	Muscle	ca. 6.8	Phosphorylase limit dextrin (glycogen) \rightarrow glucose + polysaccharide in which penultimate branches have become outer branches ⁸	Splits the α -1,6-glucosidic bonds in the branched polysaccharides glycogen and amylopectin; it acts only after a phosphorylase has degraded the outer chains of these polysaccharides exhaustively, forming a limit dextrin. By hydrolytic action, the amylo-1,6-glucosidase then liberates glucose plus a polysaccharide which can again be degraded by phosphorylase action. Successive repetitions result in complete degradation of the polysaccharide to yield glucose and glucose-1-phosphate. This enzyme differs from oligo-1,6-glucosidase in having no action on <i>iso</i> maltose, panose or α -amylase dextrin
β -Glucosidase and β -Galactosidase	Kidney ⁹ , liver ⁹ , small intestine ¹⁰ , blood	Varies with substrate	 Hydrolyze β -glucosides and β -galactosides; do not act on α -glucosides	β -Glucosidase hydrolyzes gentiobiose, cellobiose, amygdalin, salicin, prunasin and arbutin. Not affected by HCN, H_2S or glutathione, inactivated by oxidizing agents. Although this enzyme is widespread in the <i>Rosaceae</i> , molds, yeasts and bacteria, its presence in mammals is still a matter for dispute, as also its possible identity with β -galactosidase. β -Galactosidase can transfer galactose residues to a variety of acceptors (such as lactose, galactose and glucose) as well as to water, and thus can catalyze transgalactosidations

Table 13 Glycosidases (continued)

Enzyme	Location	Optimal pH of action	Reaction catalyzed	Remarks
β-Glucuronidase	Most animal tissues, especially spleen, liver and endocrine tissues ¹²	ca. 5	<div></div> <p>Hydrolyzes many glucuronides, does not act on α- or β-glucosides</p>	Dilute solutions of the enzyme show enhanced activity in presence of deoxy-ribonucleic acid. The physiological function of the enzyme probably lies in the reverse action, i.e. the formation of glucuronides. It thus plays a role in the detoxication of toxic materials and in steroid metabolism ¹¹
Hyaluronidases ¹³	Testes, semen, spleen, iris, cornea	ca. 7.5	Hydrolyze the glycosidic bonds involving the reducing group N-acetylglucosamine of hyaluronic acid. Also act on some chondroitin sulfates	Hydrolyze the mucopolysaccharide hyaluronic acid to disaccharides composed of N-acetylglucosamine and glucuronic acid, and oligosaccharides which are further hydrolyzed by β-glucuronidase. Increase the diffusion of materials injected into the skin
Sulfomucases ¹²	Testes, liver	ca. 7.5	Act primarily on chondroitinsulfuric acid by hydrolysis of the glycosidic bonds of N-acetylgalactosamine	May be part of the hyaluronidase complex of enzymes
Heparinase ¹³	Liver, kidney	5.3 – 6.8	Hydrolyzes the anti-clotting mucopolysaccharide heparin	Probably attacks the carbohydrate portion of heparin ¹³
Lysozyme ¹²	Mucus, lacrimal secretion, spleen ¹⁴	5.3	Hydrolyzes glycosidic groups in bacterial mucopolysaccharides, especially those of <i>Micrococcus lysodeikticus</i>	May play a role in defending mucous surfaces against bacterial invasion
α- and β-Glucosaminidases ¹⁵	Spleen, liver, kidney, lung, blood, heart, brain, testes	Not recorded for animal enzymes	Hydrolyze N-acetyl-α- and N-acetyl-β-glucosaminides respectively → N-acetyl-α- or N-acetyl-β-glucosamine	The β-enzyme has been shown to act on the blood-group A and O(H) substances of swine gastric mucin with the liberation of methylpentose constituents ¹⁶ . The enzyme liberates N-acetylglucosamine residues from A but not from O(H)

1) BIRD and HOPKINS, *Biochem. J.*, **56**, 86 (1954). 2) BERNFELD et al., *Helv. chim. Acta*, **33**, 1064 (1950). 3) GLOCK, G. E., *Biochem. J.*, **30**, 2313 (1936). 4) GOTTSCHALK, A., in SUMNER and MYRBÄCK (Eds.), *The Enzymes*, vol. I, part 1, New York, 1950, page 551. 5) SPRINGHORN and KOSHLAND, *Abstr. Amer. chem. Soc. 128th Meeting*, 1955, page 37 C. 6) NEUBERG and MANDL, in SUMNER and MYRBÄCK (Eds.), *The Enzymes*, vol. I, part 1, New York, 1950, page 527. 7) LARNER and McNICKLE, *J. biol. Chem.*, **215**, 723 (1955). 8) CORT, G. T., in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. I, New York, 1955, page 211. 9) NEUBERG and HOFMANN, *Biochem. Z.*, **281**, 431 (1935). 10) STEENSHOLT and VEIBEL, *Acta physiol. scand.*, **6**, 62 (1943); CLARKE et al., *J. biol. Chem.*, **131**, 135 (1939); WALLENFELS et al., *Justus Liebigs Ann. Chem.*, **584**, 63 (1953). 11) FISHMAN, W. H., in SUMNER and MYRBÄCK (Eds.), *The Enzymes*, vol. I, part 1, New York, 1950, page 635. 12) FISHMAN, W. H., in SUMNER and MYRBÄCK (Eds.), *The Enzymes*, vol. I, part 2, New York, 1951, page 769. 13) JAKUES, L. B., *J. biol. Chem.*, **133**, 445 (1940); JAKUES and CHO, *Biochem. J.*, **58**, XXV (1954). 14) JOLLÈS and FROMAGEOT, *Biobim. biophys. Acta*, **11**, 95 (1953); **14**, 219 (1954). 15) KENT and WHITEHOUSE, *Biochemistry of the Aminosugars*, London, 1955, page 20. 16) HOWE and KABAT, *J. Amer. chem. Soc.*, **75**, 5542 (1953).

Table 14 Lipases of the gastrointestinal tract

The lipases catalyze the reaction $(R\cdot CO\cdot O\cdot R')_3 + H_2O \rightleftharpoons 3R\cdot CO\cdot OH + 3HO\cdot R'$, where $R\cdot CO\cdot O$ is a long-chain fatty acid and $HO\cdot R'$ represents one of the three alcoholic groups of glycerol

Location	Optimal pH of action	Remarks
Saliva	7.5 – 7.7	Secretion from parotid gland most active ¹ . The enzyme can be found in infants as early as the first month ²
Stomach, gastric juice	Varies with substrate: 5.5 for lower triglycerides, 7.5 for higher ones ³	Stable in acid media. Present in embryo from the 7th to 8th month ⁴
Pancreas	ca. 7.8	Pancreatic lipase was formerly called <i>steapsin</i> . Activity is enhanced by presence of bile salts, proteins and soaps: this is probably the result of facilitation of enzyme–substrate interaction by emulsification of the water-insoluble substrate. Enzyme solutions are relatively unstable in aqueous media, more stable in glycerol ⁵ . Attacks tri- > di- > mono-glycerides
Intestine		Weak lipase activity of the jejunum has been reported ⁶ . Lipase appears to be absent from the ileum ⁷ . Hydrolysis of tributyrin by preparations from the large bowel is due to bacterial action; such hydrolyzed fat is not absorbed

1) KOLDAJEW and PIKUL, *Biochem. Z.*, **212**, 53 (1929). 2) SCHEER, K., *Klin. Wschr.*, **7**, 163 (1928). 3) SCHÖNHEYDER and VOLQVARTZ, *Acta physiol. scand.*, **11**, 349 (1946). 4) ITOH and KAMISASANUKI, *J. Biochem. (Tokyo)*, **33**, 269 (1941). 5) DEUEL, H. J., *The Lipids*, vol. II, London, 1955, page 9. 6) FRAZER, A. C., *Physiol. Rev.*, **26**, 103 (1946). 7) BICKEL and KANITZ, *Biochem. Z.*, **270**, 378 (1934).

Table 15 Esterases (For references see end of table, page 496)

Like the lipases, some of these enzymes catalyze the reaction $R\cdot CO\cdot OR' + H_2O \rightleftharpoons R\cdot CO\cdot OH + HOR'$, but $R\cdot CO\cdot O$ is not a long-chain fatty acid. Other esterases act on esters of acids other than carboxylic acids

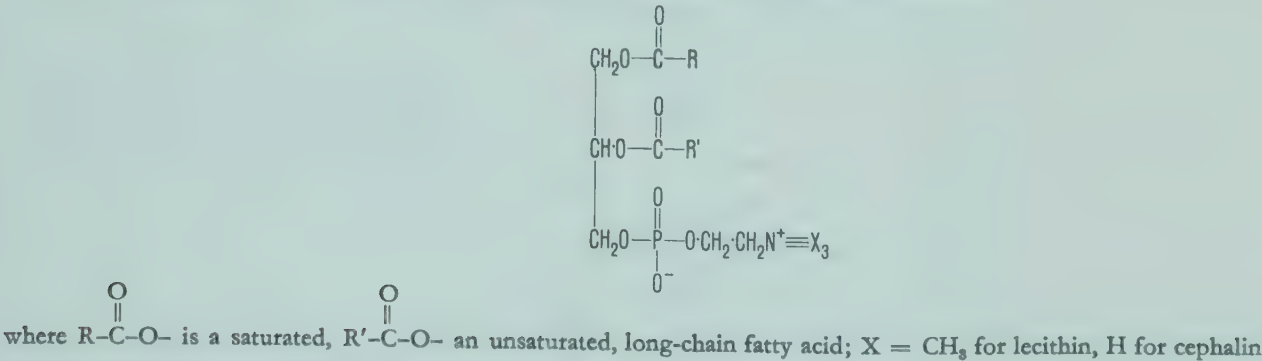
Enzyme	Location	Reaction catalyzed	Remarks
Tissue esterases (nonspecific or aliesterases)	Most tissues, highest activity in liver	Readily split most simple esters, e.g. ethyl butyrate \rightleftharpoons ethanol + butyric acid. Fats are hydrolyzed only slowly	Act more readily on simple esters than on acetylcholine. Inhibited by the hydrochloride of the <i>m</i> -dimethylaminophenyl ester of methyl-carbamic acid ¹
Choline esterases ² (a) nonspecific or pseudo	Most tissues, especially blood, pancreas, liver, ovary, placenta, heart, intestinal mucosa, skin. Not present in skeletal muscle	Split simple esters, but act more readily on those containing choline than on those not containing choline. Rate of hydrolysis increases when the acyl chain increases from 2 to 4 carbon atoms; do not act on acetyl- β -methylcholine	Inhibited by eserine, prostigmine, organophosphorus compounds. Some of these latter inhibitors act in extremely low concentrations, e.g. tetraethyl pyrophosphate effectively inhibits at a molar concentration of 10^{-10} ; this appears to be irreversible ³
(b) Specific, true or acetylcholine esterase	Most tissues, especially conductive tissues (e.g. brain, nerves), erythrocytes, skeletal muscle, adrenals, lung, liver, stomach, salivary glands	Hydrolyzes acetylcholine \rightarrow acetate + choline. Splits other choline esters also, but an increase in the acyl chain from 2 to 3 carbon atoms does not affect the rate of hydrolysis, and butyrylcholine is only slowly attacked. Rapidly splits acetyl- β -methylcholine. Also acts on non-choline esters, but at lower rates and higher concentrations	Can be distinguished from the nonspecific choline esterases by its action on acetyl- β -methylcholine ⁴ . The optimum substrate concentration for acetylcholine is 4–7 micromoles per milliliter. At higher concentrations the activity decreases. If the activity is plotted against pS (the negative logarithm of substrate concentration) a bell-shaped curve results
Phosphomonoesterases (a) Phosphomonoesterase I (alkaline phosphatase)	Most cells, particularly zones of growth of bones, intestinal mucosa, kidney cortex, mammary gland, milk, liver, brain, white blood cells, lymphoid tissue, plasma	$\begin{array}{c} OH \\ \\ O=P-O-R' \\ \\ OH \\ \\ HO-H \end{array}$	Acts optimally at pH 9.2–9.6. Activity enhanced by divalent cations, e.g. Mg^{++} , inhibited by CN^- , PO_4^{3-} , SH-compounds (e.g. cysteine). Does not attack pyrophosphates or ribonucleic acid. The enzyme also catalyzes transfer reactions, e.g. creatine phosphate + glucose \rightarrow glucose-6-phosphate + creatine. The enzymes of milk, mammary gland, kidney, bone and liver are thought to be identical, and different from that of intestinal mucosa ⁵
(b) Fructose 1,6-diphosphatase ^{6,7}	Liver	$\begin{array}{ccc} \begin{array}{c} H \quad OH \\ \quad \\ CH_2O-PO_3H_2 \\ \\ C=O \\ \\ HOCH \\ \\ HCOH \\ \\ HCOH \\ \\ CH_2O-PO_3H_2 \end{array} & \longrightarrow & \begin{array}{c} CH_2OH \\ \\ C=O \\ \\ HOCH \\ \\ HCOH \\ \\ HCOH \\ \\ CH_2O-PO_3H_2 \end{array} + H_3PO_4 \\ \text{Fructose-1,6-diphosphate} & & \text{Fructose-6-phosphate} \end{array}$ <p>Also slowly hydrolyzes fructose-1-phosphate and L-sorbose-1,6-diphosphate</p>	The enzyme is optimally active at pH 9.3–9.5; its activity is enhanced by Mg^{++} or Mn^{++} and inhibited by F^- . Does not hydrolyze glucose-1-phosphate, glucose-6-phosphate, fructose-6-phosphate, phosphoglyceric acid, L-sorbose-1-phosphate. Plays a role in the synthesis of glycogen from noncarbohydrate compounds (see Figure 14, page 515)
(c) Glucose 6-phosphatase ⁸	Liver	$\begin{array}{ccc} \begin{array}{c} HC=O \\ \\ HCOH \\ \\ HOCH \\ \\ HCOH \\ \\ HCOH \\ \\ CH_2O-PO_3H_2 \end{array} & \longrightarrow & \begin{array}{c} HC=O \\ \\ HCOH \\ \\ HOCH \\ \\ HCOH \\ \\ HCOH \\ \\ CH_2OH \end{array} + H_3PO_4 \\ \text{Glucose-6-phosphate} & & \text{Glucose} \end{array}$	Plays a role in the formation of glucose from glycogen or from noncarbohydrate compounds (see Figure 14, page 515). Absent from, or weak in, the liver during glycogen storage disease ⁹
(d) Phosphomonoesterase II (acid phosphatase)	Some tissues, particularly prostate ¹⁰ , spleen, liver, kidney, plasma	As for phosphomonoesterase I, above	Optimally active at pH 5.3–5.6. Inhibited strongly by F^- . The prostatic phosphatase is also inhibited by ethanol; the erythrocyte enzyme is not inhibited ¹¹
(e) Acyl phosphatase	Wide variety of tissues, bacteria ¹²	$R-CO-O-PO_3H_2 \longrightarrow R-COOH + H_3PO_4$ <p>where $R\cdot CO\cdot$ = acetyl, propionyl, butyryl, succinyl, octanoyl, palmityl and other acyl groups¹³</p>	Specific for acyl phosphates: does not act on α -glycerophosphate, for example. Is presumed to be a basic protein because of its solubility in acidic and its insolubility in basic solutions. Resistant to hot acidic (pH 3) solutions and to cold trichloroacetic acid. Inhibited strongly by pyrophosphate, phosphate, hexosephosphate, nucleic acid and hyaluronic acid; slightly inhibited by F^-

Table 15 Esterases (continued)

Enzyme	Location	Reaction catalyzed	Remarks
Phospho- diesterases See also Table 17 (Nucleases), page 498	Various tissues, par- ticularly intestine, spleen ¹⁴ . Also present in snake venoms	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{O}-\text{P}-\text{O}-\text{R}' \\ \\ \text{OH} \end{array} \longrightarrow \text{R}-\text{O}\cdot\text{PO}_3\text{H}_2 + \text{R}'-\text{OH}$ <p>In the body the main substrates for the phosphodiesterases are the nucleic acids (see Figure 4, page 452). Some of the phospholipases (Table 16, below) also more properly belong to this class of enzymes</p>	Mammalian enzymes are optimally active at about pH 7 ¹⁴ , and those of rattlesnake, viper water moccasin venoms ¹⁵ at pH 9.3
Inorganic pyro- phosphatase	Most tissues, particularly liver	$\begin{array}{c} \text{OH} \quad \text{OH} \\ \quad \\ \text{O}=\text{P}-\text{O}-\text{P}=\text{O} \\ \quad \\ \text{OH} \quad \text{OH} \\ \\ \text{H}\cdot\text{OH} \end{array} \longrightarrow 2 \text{H}_3\text{PO}_4$	
Pyrophos- phatases	Most tissues	$\begin{array}{c} \text{OH} \quad \text{O} \\ \quad \parallel \\ \text{R}-\text{O}-\text{P}-\text{O}-\text{P}-\text{O}-\text{R}' \\ \parallel \quad \\ \text{O} \quad \text{OH} \\ \\ \text{H}\cdot\text{OH} \end{array} \longrightarrow \text{R}-\text{O}\cdot\text{PO}_3\text{H}_2 + \text{R}'-\text{O}\cdot\text{PO}_3\text{H}_2$ <p>Examples of substrates are flavin adenine dinucleotide (FAD) and diphosphopyridine nucleotide (DPN⁺) (see Table 12, pages 460 and 461)</p>	
Phenol- sulfatases	Most tissues	Hydrolyze esters with an aromatic radical (e.g. C ₆ H ₅ ·O·SO ₃ H)	Act only on aryl esters in which the ester linkage is formed between a phenolic hydroxyl group and H ₂ SO ₄ . Optimally active at pH 6.1

1) STEDMAN and STEDMAN, *Biochem. J.*, **25**, 1147 (1931). 2) For reviews see NACHMANSOHN and WILSON, *Advanc. Enzymol.*, **12**, 259 (1951); THOMPSON, R. H. S., *Brit. med. Bull.*, **9**, 138 (1953); AUGUSTINSSON, K.-B., in SUMNER and MYRBÄCK (Eds.), *The Enzymes*, vol. I, part 1, New York, 1950, page 443. 3) MACKWORTH and WEBB, *Biochem. J.*, **42**, 91 (1948). 4) NACHMANSOHN and WILSON, in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. I, New York, 1955, page 642. 5) MORTON, R. K., in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. II, New York, 1955, page 533. 6) GOMORI, G., *J. biol. Chem.*, **148**, 139 (1943). 7) MCGILVER, R. W., in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. II, New York, 1955, page 543; POGELL and MCGILVER, *J. biol. Chem.*, **208**, 149 (1954). 8) CORI and CORI, *J. biol. Chem.*, **199**, 661 (1952). 9) FANTL and ROME, *Aust. J. exp. Biol. med. Sci.*, **23**, 21 (1945). 10) SCHMIDT, G., in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. II, New York, 1955, page 523. 11) HERBERT, F. K., *Quart. J. Med.*, **15**, 221 (1946). 12) LIPMANN, F., *Advanc. Enzymol.*, **6**, 231 (1946); SHAPIRO and WERTHEIMER, *Nature*, **156**, 690 (1945). 13) LEHNINGER, A. L., *J. biol. Chem.*, **162**, 333 (1946). 14) HEPPEL and HILMOE, in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. II, New York, 1955, page 565. 15) BUTLER, G. C., in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. II, New York, 1955, page 561.

Table 16 Phospholipases¹ (For references see end of table, page 497)
Typical phospholipids, such as lecithin or cephalin, may be represented by the general formula



Enzyme	Location	Reaction catalyzed	Remarks
Phospholipase A (lecithinase A)	Pancreas, muscles, heart, liver, kidneys, adrenals, other tis- sues ²	$\begin{array}{c} \text{CH}_2\text{O}-\text{CO}-\text{R} \\ \\ \text{CHO}-\text{CO}-\text{R}' \\ \\ \text{CH}_2\text{O}-\text{P}-\text{O}-\text{CH}_2\text{CH}_2\text{N}^+\equiv\text{X}_3 \\ \\ \text{O}^- \end{array} \longrightarrow \begin{array}{c} \text{CH}_2\text{O}-\text{CO}-\text{R} \\ \\ \text{CHOH} \\ \\ \text{CH}_2\text{O}-\text{P}-\text{O}-\text{CH}_2\text{CH}_2\text{N}^+\equiv\text{X}_3 \\ \\ \text{O}^- \end{array} + \text{R}'-\text{COOH}$	Hydrolyzes phospholipids to lysolipids, which can cause rapid hemolysis. One of the most widespread components of animal poisons, present in the poisonous secretions of snakes, echinoderms, scorpions, bees and wasps. Does not act on lipids, sphingomyelins, acetalphosphatides or cerebrosides, nor on synthetic phospholipids not containing unsaturated fatty acids. Activity enhanced by Ca ⁺⁺ . Very stable to heat: can be boiled for 5 minutes at pH 5.9 without loss of activity ³

Table 16 Phospholipases (continued)

Enzyme	Location	Reaction catalyzed	Remarks
Phospholipase B (lecithinase B)	Pancreas ¹ , other tissues ²	<div><div><div><div><div>CH₂O</div><div>CO—R</div></div><div>CHOH</div><div><div><div>O</div><div>P</div><div>O⁻</div></div><div><div>O</div><div>CH₂CH₂N⁺≡X₃</div></div></div></div><div>→</div><div><div><div>CH₂OH</div><div>CHOH</div><div><div><div>O</div><div>P</div><div>O⁻</div></div><div><div>O</div><div>CH₂CH₂N⁺≡X₃</div></div></div></div><div>+ R—COOH</div></div></div></div>	Catalyzes the hydrolytic cleavage of saturated fatty acid from lysophosphatides. Acting on lecithin, it forms glycerylphosphorylcholine, which has no hemolytic action. Less heat-stable than phospholipase A
Phospholipase C (lecithinase C)	In toxins of <i>Clostridium welchii</i> , <i>Cl. oedematiens</i> , <i>Cl. sordelli</i> . Not present in mammalian tissues	<div><div><div><div><div>CH₂O</div><div>CO—R</div></div><div>CHO—CO—R'</div><div><div><div>O</div><div>P</div><div>O⁻</div></div><div><div>O</div><div>CH₂CH₂N⁺≡X₃</div></div></div></div><div>→</div><div><div><div>CH₂O</div><div>CO—R</div></div><div>CHO—CO—R'</div><div>CH₂OH</div><div><div><div>O</div><div>P</div><div>O⁻</div></div><div><div>O</div><div>CH₂CH₂N⁺≡X₃</div></div></div></div><div>+ HO—<div><div><div>O</div><div>P</div><div>O⁻</div></div>—O—CH₂CH₂N⁺≡X₃</div></div></div></div>	Splits phospholipids at an O—P bond. Acts on lecithin, producing a diglyceride + phosphorylcholine. Attacks lecithins and sphingomyelins (which are hydrolyzed to acylsphingosine + phosphorylcholine) but not cephalins. Activity enhanced by Ca ⁺⁺ and, to a smaller degree, by Mg ⁺⁺ , Mn ⁺⁺ , Co ⁺⁺ , Zn ⁺⁺ . Rather heat-stable: retains 50% of its activity after heating at 100°C for 10 minutes
Glycerylphosphorylcholine diesterase	Not present in animal tissues, but found in some bacteria, e.g. <i>Serratia</i> ⁴	<div><div><div><div><div>CH₂OH</div><div>CHOH</div><div>CHOH</div><div>CH₂O</div><div><div><div>O</div><div>P</div><div>O⁻</div></div><div><div>O</div><div>CH₂CH₂N⁺≡X₃</div></div></div></div><div>→</div><div><div><div>CHOH</div><div>CHOH</div><div>CHOH</div><div>CH₂O</div><div><div><div>O</div><div>P</div><div>O⁻</div></div><div><div>O</div><div>OH</div></div></div></div><div>+ HO—CH₂CH₂N⁺≡X₃</div></div></div></div></div>	Hydrolyzes glycerylphosphorylcholine to glycerophosphate + choline. Also acts on glycerylphosphorylethanolamine. Optimally active at pH 8–9. Inhibited by Mg ⁺⁺ , Mn ⁺⁺ , Zn ⁺⁺ , ethylenediamine tetraacetate
Phospholipase D ⁵	Not present in mammalian tissues; has been found in carrots and cabbage	<div><div><div><div><div>CH₂—CO—R</div><div>CHO—CO—R'</div></div><div>CH₂O</div><div><div><div>O</div><div>P</div><div>O⁻</div></div><div><div>O</div><div>CH₂CH₂N⁺≡X₃</div></div></div></div><div>→</div><div><div><div>CH₂O—CO—R</div><div>CHO—CO—R'</div></div><div>CH₂O</div><div><div><div>O</div><div>P</div><div>O⁻</div></div><div><div>O</div><div>OH</div></div></div></div><div>+ HO—CH₂CH₂N⁺≡X₃</div></div></div>	Hydrolyzes the linkage between the base and phosphoric acid to form phosphatidic acid and, in the case of lecithin, choline. Heat-stable: retains 30–40% of its activity after heating at 100°C for 15 minutes

1) For a review see ZELLER, E. A., in SUMNER and MYRBÄCK (Eds.), *The Enzymes*, vol. I, part 2, New York, 1951, page 986. 2) FRANCIOLI, M., *Fermentforschung*, **14**, 241 (1935). 3) HUGHES, A., *Biochem. J.*, **29**, 437 (1935).

4) HAYAISHI, O., in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. I, New York, 1955, page 668. 5) HANAHAN and CHAIKOFF, *J. biol. Chem.*, **172**, 191 (1948).

Table 17 Nucleases (For references see end of table, page 498)

Enzyme	Location	Reaction catalyzed	Remarks
Ribonucleases ¹	Most tissues, highest activity in pancreas	Hydrolysis of ribonucleic acids	Specific phosphodiesterases which hydrolyze ribonucleic acids but not desoxyribonucleic acids. Only pancreatic ribonuclease has been studied extensively. It is a digestive enzyme with an optimum pH of 7.7. Its specificity is discussed on page 488. Studies of ribonucleases from different sources show that they vary considerably in properties such as the optimum pH
Desoxyribonucleases ²	Pancreas, thymus, spleen and various other tissues; highest activity in pancreas	Hydrolysis of desoxyribonucleic acids	Several different enzymes which hydrolyze desoxyribonucleic acid have been described, of which pancreatic desoxyribonuclease has been studied most extensively. The enzyme hydrolyzes desoxyribonucleic acids but not ribonucleic acid. Its specificity is discussed on page 488

Table 17 Nucleases (continued)

Enzyme	Location	Reaction catalyzed	Remarks
Phosphodiesterases	Intestine, spleen and other tissues	Hydrolysis of nucleic acid fragments	Discussed under esterases (Table 15, page 496)
5'-Nucleotidase ³	Seminal plasma	Hydrolysis of adenylic acid, inosinic acid, uridylic acid, cytidylic acid and nicotinamide mononucleotide to the corresponding nucleosides and orthophosphate	Desoxyribonucleotides are also attacked by this enzyme
Nucleoside phosphorylase ⁴	Liver, muscle, spleen	Nucleoside + orthophosphate → pentose-1-phosphate + purine or pyrimidine	Desoxyribonucleosides are also attacked by this enzyme ⁵
Adenylic deaminase ^{6,7}	Muscle and to a much lesser extent in other tissues	Deaminates adenylic acid to inosinic acid and ammonia	Specific for 5'-adenylic acid (adenosine 5'-monophosphate); optimum pH of 5.9. Activated by citrate, chloride and other anions
Guanylic deaminase ⁸	Liver	Deaminates guanylic acid to xanthidylic acid and ammonia	
Adenosine deaminase ^{6,7,9}	Muscle, liver, intestinal mucosa and other tissues	Deaminates adenosine to inosine and ammonia	Desoxyadenosine is also deaminated by the enzyme. Broad optimum pH range between 6 and 9
Guanosine deaminase ^{9,10}	Liver	Deaminates guanosine to xanthosine and ammonia	
Guanase ^{6,8}	Liver, muscle	Deaminates guanine to xanthine and ammonia	Guanosine and guanylic acid are not attacked by this enzyme. Acts optimally from pH 6 to 10
Xanthine oxidase ¹¹	Milk, liver, spleen, kidney, lung	The purified enzyme oxidizes hypoxanthine to xanthine, xanthine to uric acid, and aldehydes to acids	Contains flavin adenine dinucleotide, iron and molybdenum
Uricase ¹²	Liver and kidney of mammals. Absent in man and other primates	Oxidizes uric acid to allantoin according to the overall reaction: uric acid + O ₂ + 2 H ₂ O → allantoin + H ₂ O ₂ + CO ₂	Contains copper

1) McDONALD, M. R., in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. II, New York, 1955, page 427. 2) McDONALD, M. R., in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. II, New York, 1955, page 437. 3) HEPPEL and HILMOE, in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. II, New York, 1955, page 546. 4) PRICE et al., in COLOWICK and KAPLAN (Eds.), *Methods in Enzymology*, vol. II, New York, 1955, page 448. 5) FRIEDKIN and KALCKAR, *J. biol. Chem.*, **184**, 437 (1950). 6) KALCKAR, H. M., *J. biol. Chem.*, **167**, 461 (1947). 7) SCHMIDT, G., *Hoppe-Seyl. Z. physiol. Chem.*, **179**, 243 (1928). 8) SCHMIDT, G., *Hoppe-Seyl. Z. physiol. Chem.*, **208**, 185 (1932). 9) KORNBERG and PRICER, jr., *J. biol. Chem.*, **193**, 481 (1951). 10) WAKABAYASHI, Y., *J. Biochem. (Tokyo)*, **28**, 185 (1938). 11) MAHLER, H. R., *Advanc. Enzymol.*, **17**, 233 (1956). 12) MAHLER et al., *Science* **124**, 705 (1956).

Apart from supplying energy, the products of digestion serve as precursors of many cell constituents. The mammalian body can form all cell constituents from:

- 1. The essential amino acids (see pages 224–225)
- 2. The vitamins (see pages 209–223)
- 3. The essential (highly unsaturated) fatty acids
- 4. Mineral salts
- 5. A bulk source of carbon (usually carbohydrate)
- 6. A source of nitrogen in the form of ammonia derived mainly from surplus amino acids, with small amounts supplied by purine bases, pyrimidines and amino sugars.

Carbohydrate as a bulk source of carbon can be largely replaced by protein and fat, especially in carnivores.

Much progress has been made in recent years in the elucidation of the pathways by which the basic constituents of food are con-

verted into cell constituents, but many details still remain to be clarified. A synopsis of the available information is contained in the section which follows.

1. Formation of basic cell constituents and metabolites from glucose

The principal products, their pathways of formation and their physiological functions are summarized in Table 18 below.

The pentose-phosphate cycle

Glucose-6-phosphate (formed from glucose by the hexokinase reaction) can be oxidized in liver and some other animal tissues at the carbon atom 1 to yield 6-phosphogluconate. This initiates a sequence of reactions in which various pentose-phosphates and other sugar phosphates are formed. In the course of these reactions

Table 18 Formation of basic cell constituents and metabolites from glucose
This list is not comprehensive

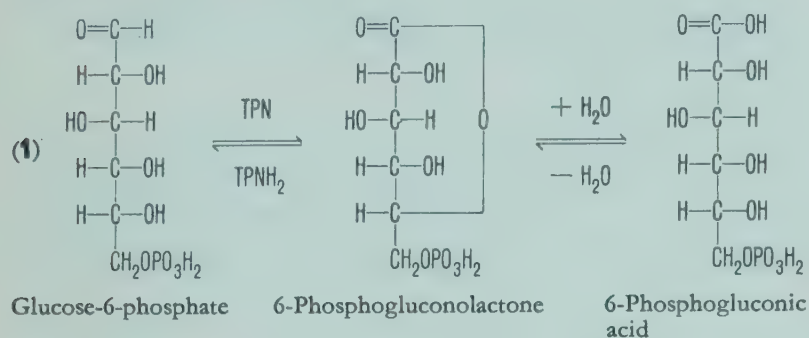
Product formed	Pathway of formation	Physiological function
Glycogen	Reversal of two stages of glycolysis (reactions catalyzed by phosphorylase and phosphoglucomutase; see Table 4, page 473, reactions 1 and 2)	Storage of energy
Galactose	Reversal of reactions 4 and 5, Table 4, page 473	Constituent of lactose, cerebrosides
Lactose	Probably from uridine diphosphogalactose and glucose-1-phosphate, via lactose-1-phosphate ¹	Milk constituent
Ribose-5-phosphate	Reactions of the pentose-phosphate cycle (page 500)	Constituent of nucleic acid and nucleotides
Desoxyribose-5-phosphate	Probably by aldol condensation between glyceraldehyde phosphate and acetaldehyde (reversal of the reaction shown on page 482)	Constituent of nucleic acids
Glucuronic acid	Formed via uridine diphosphoglucose (see page 501)	Constituent of mucins (hyaluronic acid and chondroitin sulfate) and of heparin; detoxicating agent
Fructose	Reactions of glycolysis and hydrolysis of fructose-6-phosphate by phosphatase	Constituent of semen
Citric acid	CO ₂ -fixation by pyruvate (see page 502) and reactions of the tricarboxylic acid cycle (see page 474)	Constituent of bone, milk, semen
Fatty acids	From acetyl-coenzyme A (formed via pyruvate) by reversal of the reactions causing the degradation of fatty acids (see page 474)*	Constituents of fats and phospholipids
Glycerophosphates	Reduction of dihydroxyacetone phosphate, catalyzed by glycerophosphate dehydrogenase	Constituents of phospholipids
Phospholipids	See page 502	Cell constituents
Glyceride fats	See page 503	Cell constituents
Sterols and steroids	See pages 503–507	Cell constituents; hormones
Nonessential amino acids:		
Glutamic acid	Glutamic dehydrogenase reaction (see page 507)	Constituent of proteins and special peptides (glutathione, folic acid)
Aspartic acid	CO ₂ -fixation by pyruvate (see page 502) and transamination between glutamate and oxaloacetate	Constituent of proteins
Alanine	Transamination between pyruvate and glutamate	Constituent of proteins
Glycine	From 3-phosphoglycerate by reactions shown on page 507	Constituent of proteins
Serine		Constituent of proteins
Cysteine	From serine by transsulfuration from homocysteine derived from methionine (see page 480)	Constituent of proteins
Proline	From glutamic acid or ornithine (see page 507)	Constituent of proteins
Hydroxyproline	Probably by oxidation of proline (see page 507)	Constituent of proteins

* Although the intermediates in the fatty-acid synthesis from acetyl-coenzyme A are the same as those occurring in the reverse process, the enzymic mechanisms of synthesis and breakdown are different. Cf. WAKIL et al., *Biochim. biophys. Acta*, **34**, 227 (1959).

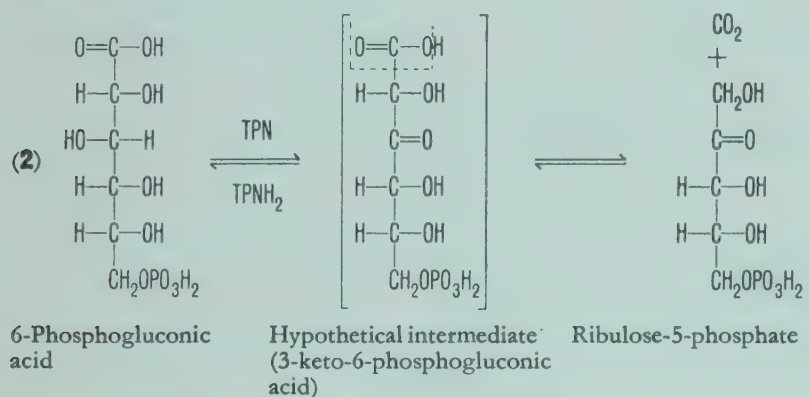
1) GANDER et al., *Arch. Biochem. Biophys.*, **60**, 259 (1956); PAZUR and TIPTON, *J. biol. Chem.*, **224**, 381 (1957).

some glucose-6-phosphate is regenerated, implying a cyclic nature of the reaction sequence. The reactions of this cycle represent a partial oxidation of glucose-6-phosphate.

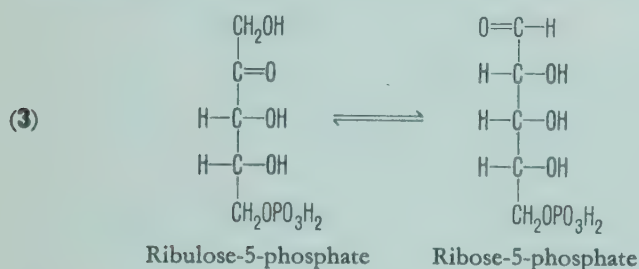
The main components of the cycle are eight different reactions. In the first reaction (1) glucose-6-phosphate is oxidized to 6-phosphogluconolactone, which is subsequently hydrolyzed by a "lactonase" to 6-phosphogluconate¹. TPN is reduced in this reaction.



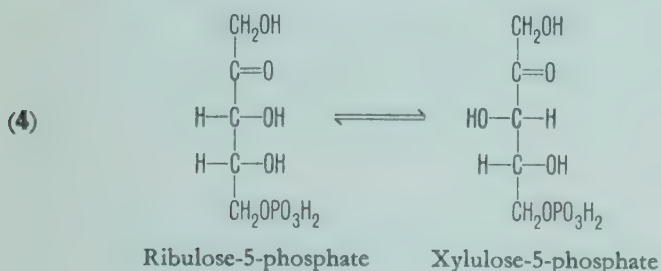
The 6-phosphogluconate formed is oxidatively decarboxylated (2) to yield ribulose-5-phosphate, whilst another molecule of TPN is reduced²:



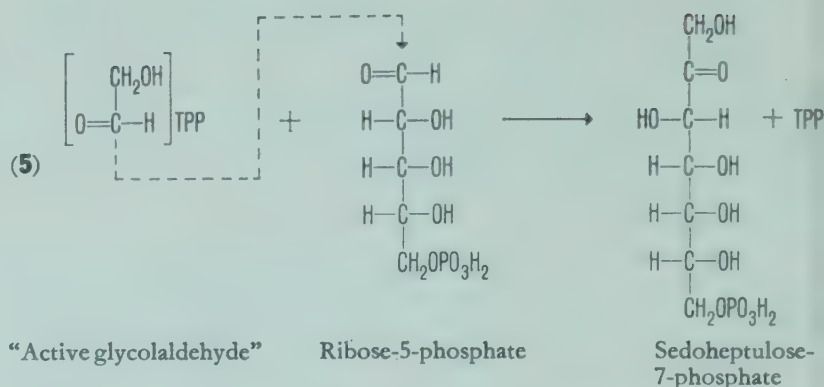
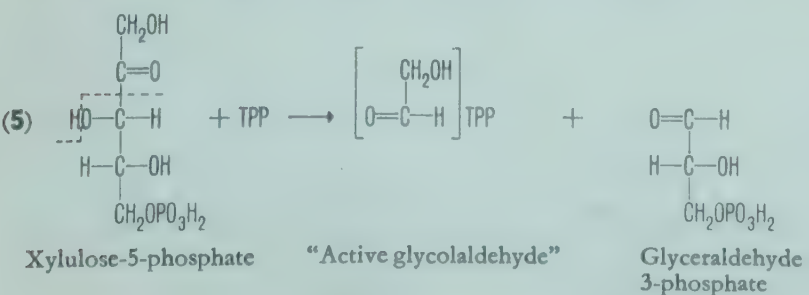
Ribulose-5-phosphate undergoes two different isomerizations, one to ribose-5-phosphate (3) catalyzed by pentose-phosphate isomerase³:



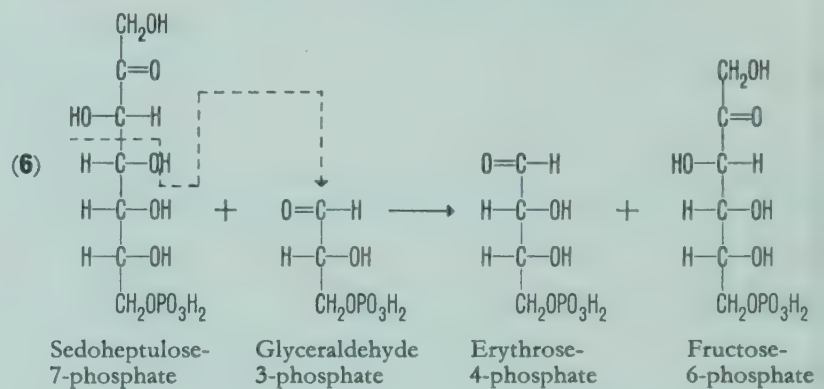
and one (4) to xylulose-5-phosphate^{4,5}:



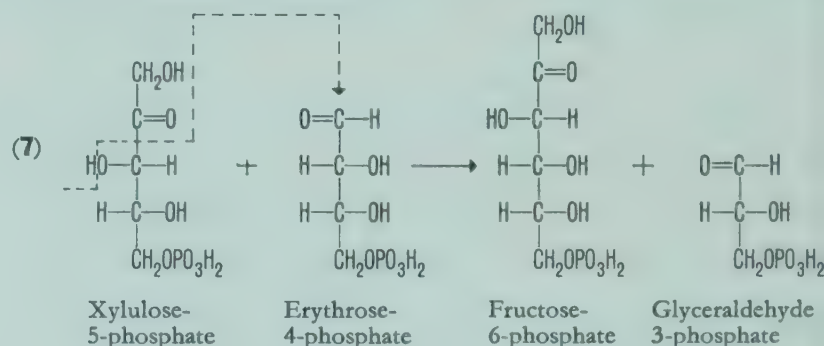
One molecule of xylulose-5-phosphate and one of ribose-5-phosphate, produced by reactions (3) and (4), interact to form sedoheptulose-7-phosphate and glyceraldehyde 3-phosphate (5)^{4,6}. This reaction is catalyzed by transketolase⁷, an enzyme requiring thiamine pyrophosphate (TPP) as co-factor. It is thought that an "active glycolaldehyde" may be an intermediate in this reaction. This may therefore be written as:



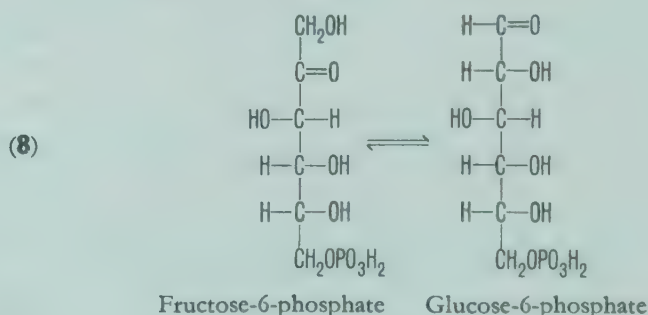
The glyceraldehyde 3-phosphate and sedoheptulose-7-phosphate interact further in a transfer reaction under the influence of transaldolase. The action of this enzyme is analogous to that of transketolase, except that the moiety transferred is not an "active glycolaldehyde" but an "active dihydroxyacetone". In this reaction (6) fructose-6-phosphate and erythrose-4-phosphate are formed⁸:



The erythrose-4-phosphate formed in (6) undergoes a transketolase reaction (7) with a molecule of xylulose-5-phosphate. This is analogous to reaction (5) and leads to fructose-6-phosphate and glyceraldehyde 3-phosphate⁹:



The fructose-6-phosphate formed in reactions (6) and (7) is converted to glucose-6-phosphate by reaction (8), catalyzed by hexose-phosphate isomerase:



This reaction completes the cycle in that it leads to the (partial) regeneration of the starting material, glucose-6-phosphate. The interplay of the components of the cycle is somewhat complex. It is shown diagrammatically in Figure 10 and Table 19 (see page 501).

In this scheme, the reactions catalyzed by transketolase and transaldolase, (5), (6) and (7), are indicated by crossing arrows; of the three glucose-6-phosphate molecules required for each turn of the cycle, two are regenerated. While three molecules participate in reactions (1) and (2), two are involved in reactions (4) and (8) and only one each participates in the remaining reactions.

The net effect of one revolution of the cycle, as shown in Table 19, is therefore:



Table 19 The component reactions of the pentose-phosphate cycle and their quantitative relations

(1)	3 glucose-6-phosphate + 3 TPN	(glucose-6-phosphate dehydrogenase) →	3 6-phosphogluconate + 3 TPNH ₂
(2)	3 6-phosphogluconate + 3 TPN	(6-phosphogluconate dehydrogenase) →	3 ribulose-5-phosphate + 3 CO ₂ + 3 TPNH ₂
(3)	ribulose-5-phosphate	(pentose-phosphate isomerase) →	ribose-5-phosphate
(4)	2 ribulose-5-phosphate	(xylulo-waldenase) →	2 xylulose-5-phosphate
(5)	ribose-5-phosphate + xylulose-5-phosphate	(transketolase) →	sedoheptulose-7-phosphate + glyceraldehyde 3-phosphate
(6)	sedoheptulose-7-phosphate + glyceraldehyde 3-phosphate	(transaldolase) →	fructose-6-phosphate + erythrose-4-phosphate
(7)	xylulose-5-phosphate + erythrose-4-phosphate	(transketolase) →	fructose-6-phosphate + glyceraldehyde 3-phosphate
(8)	2 fructose-6-phosphate	(hexose-phosphate isomerase) →	2 glucose-6-phosphate
Sum:	glucose-6-phosphate + 6 TPN	→	3 CO ₂ + glyceraldehyde 3-phosphate + 6 TPNH ₂

The glyceraldehyde 3-phosphate thus formed does not, however, accumulate in the organism. It can be converted into pyruvate and acetyl-coenzyme A and undergo complete oxidation. Alternatively, if triose-phosphate isomerase, aldolase, fructose 1,6-diphosphatase and hexose-phosphate isomerase are present, the following sequence of reactions can occur:

- (9) glyceraldehyde 3-phosphate → dihydroxyacetone phosphate
 glyceraldehyde 3-phosphate
 (10) + dihydroxyacetone → fructose-1,6-diphosphate phosphate
 (11) fructose-1,6-diphosphate → fructose-6-phosphate + H₂O → + H₃PO₄
 (8) fructose-6-phosphate → glucose-6-phosphate

Glucose-6-phosphate would thus be formed from two molecules of glyceraldehyde 3-phosphate, and could re-enter (and be oxidized by) the pentose-phosphate cycle. Reactions (1)–(11) repeated several times would therefore result in a complete combustion of glucose-6-phosphate. This concept, which rests on the demonstration of all the required enzymes in liver¹⁰, is illustrated in Figure 11.

Fig. 11 Complete oxidation of glucose-6-phosphate via the pentose-phosphate cycle and additional reactions catalyzed by triose-phosphate isomerase, aldolase, fructose 1,6-diphosphatase and hexose-phosphate isomerase.

The first step shown in the diagram (conversion of glucose-6-phosphate into glyceraldehyde phosphate + 3 CO₂) represents the sum of the reactions shown in Table 19 and Figure 10. P = phosphate

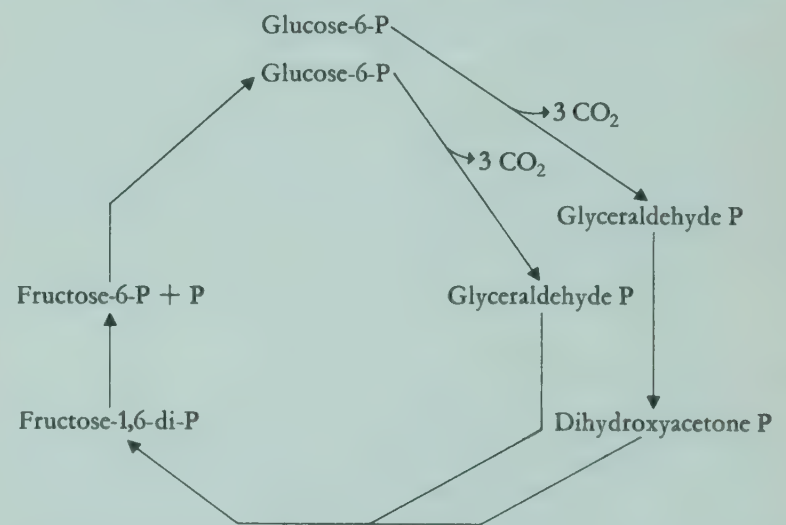
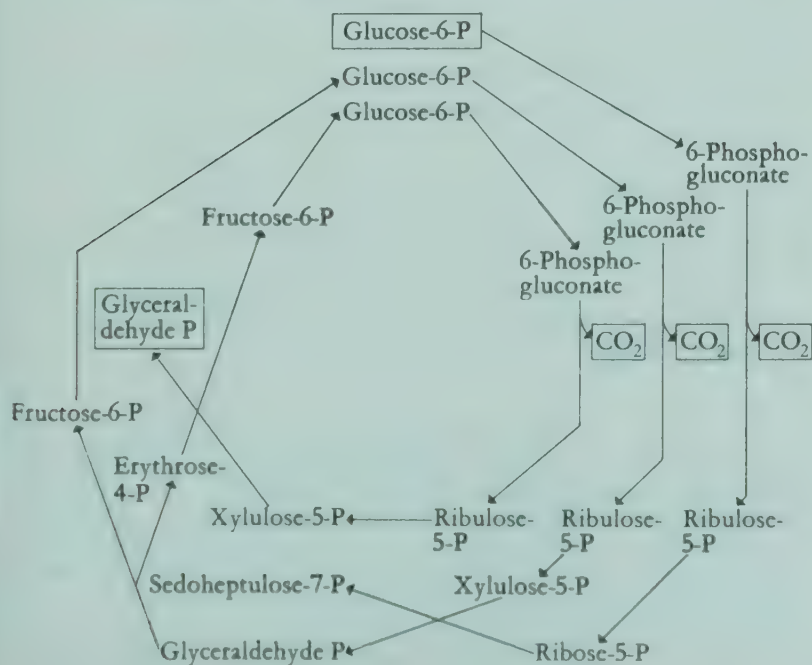


Fig. 10 Diagram of the pentose-phosphate cycle

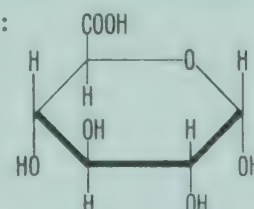
Starting materials and end-products are shown enclosed. P = phosphate. The crossing arrows indicate transfer reactions. For further details see Table 19 and the text



- 1) WARBURG and CHRISTIAN, *Biochem. Z.*, **287**, 440 (1936); CORI and LIPMANN, *J. biol. Chem.*, **194**, 417 (1952). 2) WARBURG and CHRISTIAN, *Biochem. Z.*, **292**, 287 (1937); HORECKER et al., *J. biol. Chem.*, **193**, 383 (1951). 3) AXELROD et al., *J. biol. Chem.*, **202**, 619 (1953). 4) SRERE et al., *Arch. Biochem. Biophys.*, **59**, 535 (1955). 5) DICKENS and WILLIAMSON, *Nature*, **176**, 400 (1955). 6) HORECKER et al., *J. Amer. chem. Soc.*, **78**, 692 (1956). 7) RACKER et al., *J. Amer. chem. Soc.*, **75**, 1010 (1953); DE LA HABA et al., *J. biol. Chem.*, **214**, 409 (1955). 8) HORECKER and SMYRNIOTIS, *J. Amer. chem. Soc.*, **75**, 2021 (1953); HORECKER et al., *J. biol. Chem.*, **212**, 827 (1955); SRERE et al., *Fed. Proc.*, **14**, 285 (1955). 9) KORNBERG and RACKER, *Biochem. J.*, **61**, iii (1955). 10) HORECKER et al., *J. biol. Chem.*, **207**, 393 (1954); GIBBS and HORECKER, *J. biol. Chem.*, **208**, 813 (1954).

Formation of glucuronic acid

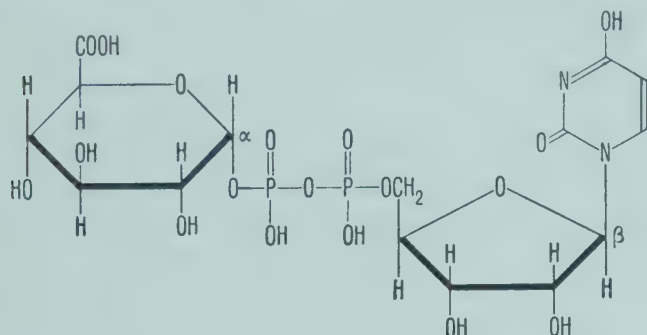
This acid:



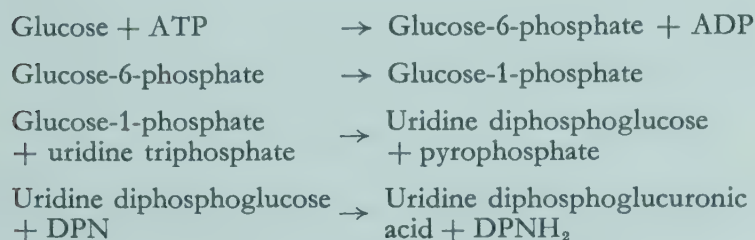
is a constituent of mucopolysaccharides as well as a coupling agent in detoxication reactions. It couples with many substances possessing hydroxyl groups, such as alcohols and substances which in the body are converted into alcohols (salicylic acid, camphor,

menthol, chloral hydrate, pregnanediol) or phenols (phenol, indoxyl). It also couples with carboxyl groups attached to an aromatic nucleus (benzoic acid, phenylacetic acid)¹, and with bile pigments².

The reactive form of glucuronic acid in the conjugation reactions, and probably also in the synthesis of mucopolysaccharides, is uridine diphosphoglucuronic acid:



This arises from glucose by the following reactions³:



The synthesis of conjugated glucuronide may be represented as follows⁴:

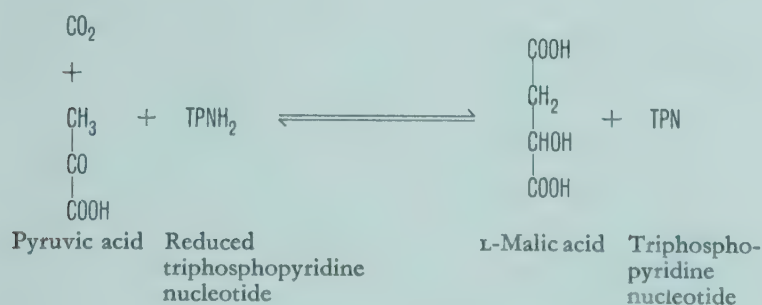


where ROH is an alcoholic or phenolic compound, or an aromatic carboxylic acid.

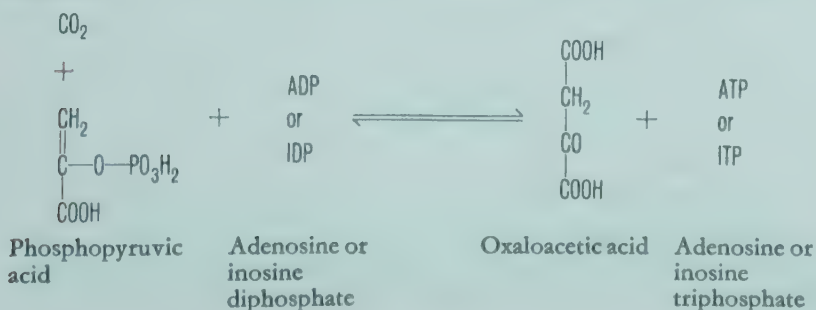
1) WILLIAMS, R. T., *Detoxication Mechanisms*, London, 1947. 2) BILLING and LATHE, *Biochem. J.*, **63**, 6P (1956). 3) STROMINGER et al., *J. Amer. chem. Soc.*, **76**, 6411 (1954). 4) STOREY and DUTTON, *Biochem. J.*, **59**, 279 (1955); SMITH and MILLS, *Biochim. biophys. Acta*, **13**, 386 (1954).

Extension of carbon chains by carbon dioxide fixation

An important link in the building-up of the carbon skeletons of cell constituents is the addition of CO₂ to pyruvate. There are at least two CO₂-fixation reactions in animal tissues by which 4-carbon chains arise from pyruvate. The first¹ is catalyzed by the "malic" enzyme; it requires reduced triphosphopyridine nucleotide and leads to L-malic acid:



The second reaction² requires adenosine diphosphate or inosine diphosphate and consists of the binding of CO₂ by phosphopyruvate (reaction of UTTER and KURAHASHI); it leads to oxaloacetate:

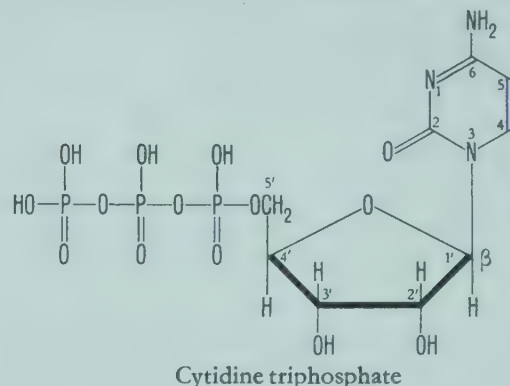


Both reactions readily occur in liver tissue and also elsewhere. They are reversible. The malic and oxaloacetic acids formed can enter the tricarboxylic acid cycle and form citrate and α-ketoglutarate.

1) OCHOA et al., *J. biol. Chem.*, **174**, 979 (1948); VEIGA SALLES and OCHOA, *J. biol. Chem.*, **187**, 849 (1950); HARARY et al., *J. biol. Chem.*, **203**, 595 (1953). 2) UTTER and KURAHASHI, *J. biol. Chem.*, **207**, 821 (1954).

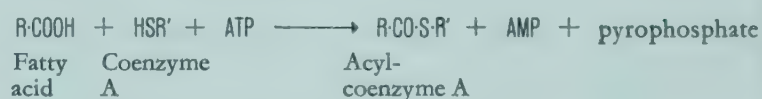
Formation of lecithin and cephalin

The synthesis of lecithin in animal tissues from fatty acids, glycerophosphate and choline requires the participation as cofactors of ATP, coenzyme A and cytidine triphosphate:



The intermediary stages of the synthesis are as follows:

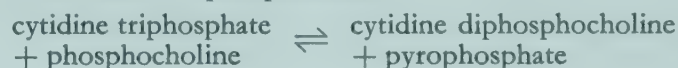
(a) "Activation" of fatty acids¹:



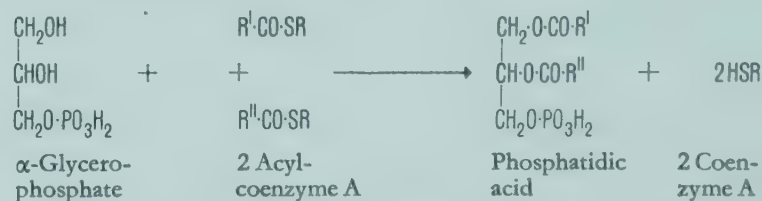
(b) "Activation" of choline by choline phosphokinase²:



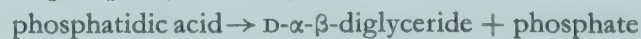
(c) "Activation" of phosphocholine³:



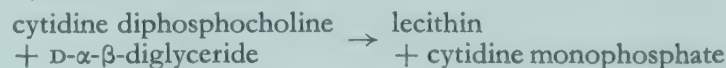
(d) Synthesis of phosphatidic acid³:



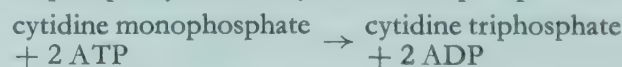
(e) Dephosphorylation of phosphatidic acid³:



(f) Synthesis of lecithin³:



(g) Rephosphorylation of cytidine monophosphate⁴:

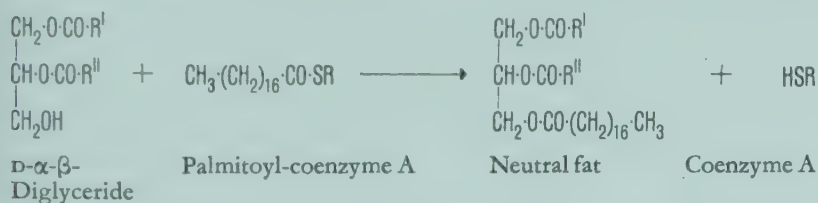


Cephalin is synthesized by analogous reactions, choline being replaced by ethanolamine (HO·CH₂·CH₂·NH₂).

1) KORNBERG and PRICER, *J. biol. Chem.*, **204**, 329 (1953). 2) WITTENBERG and KORNBERG, *J. biol. Chem.*, **202**, 431 (1953). 3) WEISS et al., *Nature*, **178**, 594 (1956); KENNEDY and WEISS, *J. Amer. chem. Soc.*, **77**, 250 (1955); KENNEDY and WEISS, *J. biol. Chem.*, **222**, 193 (1956); KENNEDY, E. P., *J. biol. Chem.*, **222**, 185 (1956). 4) BERG and JOKLIK, *J. biol. Chem.*, **210**, 657 (1954); KREBS and HEMS, *Biochim. biophys. Acta*, **12**, 172 (1953); KREBS and HEMS, *Biochem. J.*, **61**, 435 (1955); LIEBERMAN et al., *J. biol. Chem.*, **215**, 429 (1955); BRUMM et al., *J. biol. Chem.*, **220**, 713 (1956).

Formation of neutral fat

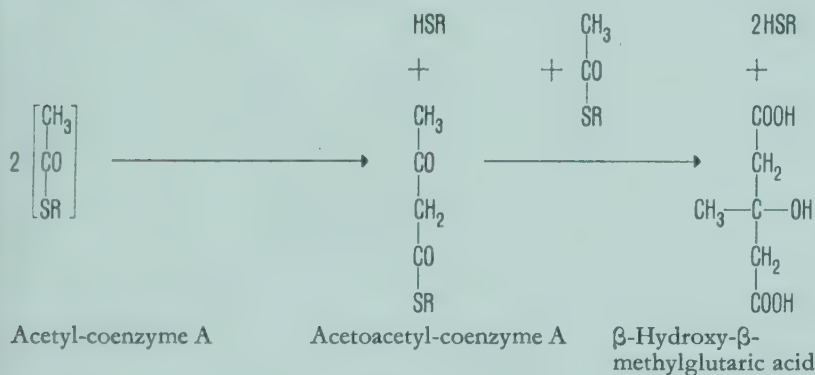
WEISS and KENNEDY¹ have presented evidence which suggests that the glycerol moiety of neutral fat is derived from α -glycerophosphate and that the reactions (d) and (e) of the preceding section (the synthesis of phosphatidic acid and its dephosphorylation) are also intermediary stages in the synthesis of neutral fat. They showed that liver preparations catalyze the following reaction:



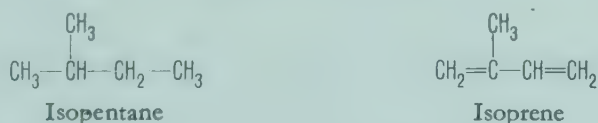
1) WEISS and KENNEDY, *J. Amer. chem. Soc.*, **78**, 3550 (1956).

Formation of cholesterol

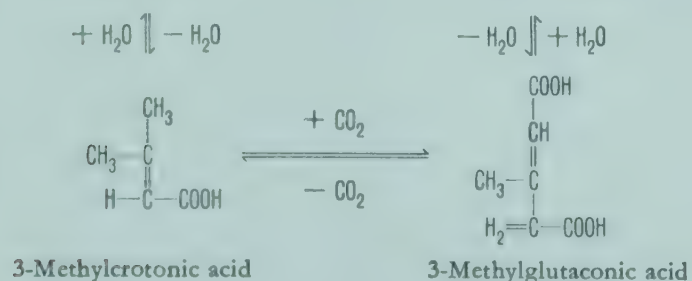
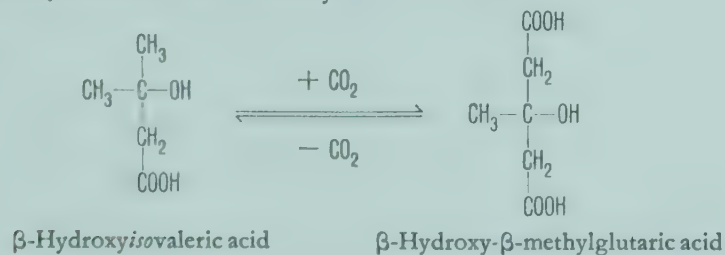
The entire carbon skeleton of cholesterol can be synthesized in the animal body, particularly in the liver, from acetate. Many details of the intermediary stages are still unknown, but a broad outline of the pathway of synthesis has recently emerged¹. The first stage is probably the formation of acetoacetyl-coenzyme A from two molecules of acetyl-coenzyme A, followed by the condensation of a further acetyl-coenzyme A molecule with acetoacetyl-coenzyme A to form β -hydroxy- β -methylglutaric acid or some closely related C_6 structure:



In some manner as yet obscure, this C_6 compound provides the C_6 isopentane-type structural unit which is the basis of the carbon skeleton of cholesterol and which appears as the "isoprene" unit in a number of isoprenoid intermediates.

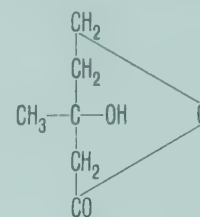


The above condensation reactions leading to β -hydroxy- β -methylglutaric acid are readily reversible, and in most systems the compound is also in equilibrium with 3-methylglutaconic, 3-hydroxyisovaleric and 3-methylcrotonic acids:



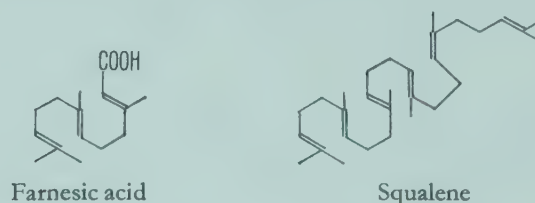
The rapid interconversion of these substances has made their study as precursors of cholesterol extremely difficult and their status as intermediates is still in doubt.

β -Hydroxy- β -methyl- δ -valerolactone ("mevalonic acid") is a C_6 derivative which is closely related structurally to β -hydroxy- β -methylglutaric acid and is probably more closely related to the C_5 isopentane building unit than any other substance which has been tested, since it is a far more efficient and direct precursor of cholesterol than any of the compounds mentioned above^{2,3}.



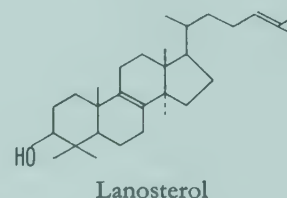
β -Hydroxy- β -methyl- δ -valerolactone ("mevalonic acid")

The concept that the skeleton of cholesterol has a basically "isoprenoid" structure implies the formation of intermediates with carbon atoms numbering multiples of five*. The C_{15} compound farnesic acid and the C_{30} compound squalene have so far been shown to behave like intermediates.

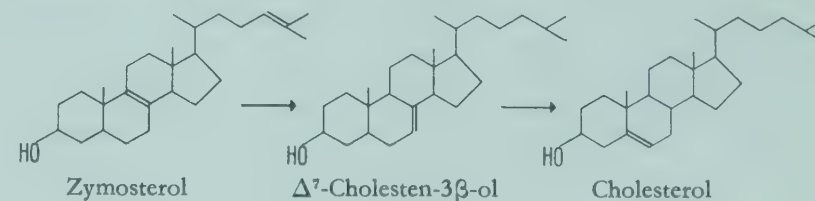


The theory that the initial condensing unit for the formation of these isoprenoid compounds may be isoprene itself has not received experimental support. The C_6 compound δ -valerolactone gives rise to squalene by some mechanism which apparently does not involve the intermediate formation of free isoprene³.

Farnesic acid and squalene are both formed in liver homogenates from acetate, and squalene can react further in the liver to form cholesterol. The carbon skeleton of farnesic acid represents one half of the symmetric structure of squalene. Squalene in turn can be cyclized by enzymes of liver tissue to give a C_{30} trimethylsterol, lanosterol⁴:



which can react to yield the C_{27} compound cholesterol, probably via zymosterol and Δ^7 -cholesten- 3β -ol.



* The syntheses of many other compounds occurring in plants and microorganisms can be explained by the assumption that they involve the same C_5 repeating unit. Substances consisting of 2, 3, 4 and 6 of these C_5 units are called mono-, sesqui-, di-, and tri-terpenes respectively. Examples are essential oils (citral, limonene), pigments (carotene, lycopene), vitamin A, camphor and rubber.

1) FRIEDMAN et al., *Ann. Rev. Biochem.*, **25**, 613 (1956). 2) TAVORMINA et al., *J. Amer. chem. Soc.*, **78**, 4498 (1956). 3) CORNFORTH et al., *Biochem. J.*, **69**, 146 (1958). 4) TCHEN and BLOCH, *J. Amer. chem. Soc.*, **77**, 6085 (1955).

Synthesis and metabolism of the steroids of the adrenal cortex

The adrenal cortex is more versatile than any other tissue in its capacity to synthesize steroid hormones. Besides producing eight C_{21} steroids of known structure and proven "corticoid" activity, it also produces at least fifteen other known C_{21} steroids the physiological activity of which is not known, as well as progesterone, the estrogens and the androgens of the C_{19}O_2 and C_{19}O_3 series.

The C_{21} corticoids exert profound effects on carbohydrate and protein metabolism ("glucocorticoid" activity) and upon sodium and potassium metabolism ("mineralocorticoid" activity). Most of these compounds exert effects of both types with one or the other predominating, according to the chemical structure¹. The more powerful glucocorticoids are those having oxygen functions at both C-11 and C-17. The glucocorticoid action of the adrenal is considered to be accounted for almost wholly by the cortisol (hydrocortisone) which it produces, since this is both the most potent naturally occurring steroid in this respect and also the most abundant product of the adrenal cortex. Corticosterone, the second most abundant corticoid, has a less powerful glucocorticoid action. The most potent hormone in the regulation of salt metabolism is aldosterone, a quantitatively minor product. Desoxycorticosterone has a much smaller but still detectable effect on salt metabolism. For further discussion of the adrenocortical steroids see page 203.

Figure 12 (page 504) shows the most probable routes²⁻⁴ of biosynthesis of the physiologically active C_{21} steroids of the adrenal and of its four principal C_{19} androgenic products. It is based very largely on studies *in vitro* with bovine adrenal tissue but evidence from studies *in vivo* in man is consistent with the operation of the pathways shown⁵.

It has been established^{3,4} that cholesterol can give rise to all the C_{21} steroid hormones, the first identifiable C_{21} product being pregnenolone which is then converted to progesterone. From progesterone two main divergent pathways appear to be available, depending upon whether hydroxylation takes place first at the 17 α -position (giving 17 α -hydroxyprogesterone) or at the 21-position (giving desoxycorticosterone). Most of the data indicate that hydroxylation at C-17 proceeds more readily in the absence of the 21-hydroxy group, though 17 α -hydroxylation of 21-hydroxy compounds has been observed. Both desoxycorticosterone and 17 α -hydroxydesoxycorticosterone may undergo hydroxylation at the 11 β -position, giving respectively corticosterone and cortisol which on further oxidation at C-11 yield minor amounts of two further physiologically active substances, 11-dehydrocorticosterone and cortisone. The pathway to aldosterone is still not clear but its formation from desoxycorticosterone has been demonstrated⁶, as has the hydroxylation of desoxycorticosterone to the hypothetical intermediate 18-hydroxydesoxycorticosterone⁷, which could yield aldosterone by 11 β -hydroxylation and further oxidation at C-18. The origin of the androgens is discussed below under Oxidative degradation.

There is evidence of an alternative pathway of synthesis which bypasses cholesterol^{3,4} but probably involves an unknown precursor common to cholesterol and the hormones. However, nothing is yet known of the details of this alternative pathway of synthesis. There is evidence that it is independent of control by ACTH (see below).

Pituitary control. The adrenal cortex is maintained in a normally functional state by the action of pituitary ACTH. Aside from this generalized influence on the metabolism of adrenal cortical tissue, ACTH also exerts a specific and immediate stimulating effect upon the process of corticosteroid biogenesis. The precise point (or points) at which this influence is exerted is still in doubt. One important point of action is considered to be at a very early stage, probably in the conversion of cholesterol to pregnenolone⁸. It has also been observed^{8,9} that ACTH stimulation can alter the ratio of cortisol to corticosterone secreted, but such an effect does not necessarily imply intervention of ACTH in the later stages of biosynthesis. Cortisol itself is a powerful depressant of ACTH secretion and hence it appears that a homeostatic control operates between the pituitary and the adrenal cortex.

Aldosterone. Aldosterone, so named on account of its aldehydic group at C-18¹⁰, has an influence on salt metabolism which is extremely powerful by comparison with that of other known salt-active corticoids. In sodium-retention tests its effect is 25–100 times that of desoxycorticosterone¹¹ without parallel effect on water loss. Aldosterone also has an effect on carbohydrate metabolism, with a positive glycogen deposition reaction in the mouse of approximately 30 times that of desoxycorticosterone¹² and life-maintenance activity in the dog and rat^{10,13} of a similar order compared with that of desoxycorticosterone. Doses of the order [of 3 μ g/per day/per kilogram body weight] relieve the clinical symptoms of ADDISON's disease¹⁴. The influence on nitrogen metabolism in the doses so far administered has been negligible. The clinical conditions of primary hyperaldosteronism¹⁵ and primary hypoaldosteronism¹⁶ have been described.

The available evidence¹⁷ indicates only a minor control of aldosterone secretion by ACTH, since aldosterone output falls by only about 30% after hypophysectomy¹⁸. More important and direct is probably the control by the sodium and potassium concentrations and the extracellular fluid volume of the body. The excretion of aldosterone in the urine takes place in a well-defined inverse ratio to the urinary sodium content¹⁷. It has also been proposed¹⁹, on the basis of experiments with partially decapitated dogs in which head circulation was artificially maintained independently of that of the body, that there is a center in the brain responsive to extracellular fluid volume changes which mediates in the homeostasis of aldosterone output. Aldosterone is excreted in the urine partly in the free state and partly in glucuronide form¹⁹.

Catabolism of the steroids of the adrenal cortex

The physiologically active corticoids shown in Figure 12 undergo a multiplicity of further transformations^{2,20} both in the adrenal itself and in the other tissues, notably the liver and sex glands. It is not known at present whether these transformations are related to the hormonal function of these compounds. The catabolic reactions may be classified in three principal groups: oxidative degradation, hydroxylation, and reduction.

Oxidative degradation. The cleavage of the side chain of the C_{21} steroids having the 17 α -hydroxy-20-keto grouping is probably the main route by which the adrenal androgens arise and may well represent a key reaction in the synthesis of androgens by the testis²¹ and of estrogens by the ovary²². It is on account of this cleavage reaction that urinary 17-ketosteroid excretion may be taken as a rough index of adrenocortical activity (see 17-Ketosteroids, page 200). Under this heading may also be included the oxidation of the 17 β -hydroxy group of testosterone to the 17-ketone (Δ^4 -androstene-3,17-dione). This reaction links testosterone, a product peculiar to the testis, with the range of C_{19} metabolites shown as derivatives of the adrenal androgens in Figure 12 on page 504.

Hydroxylation. Besides the hydroxylations at C-11, C-17 and C-21 which lead to the formation of the active C_{21} corticoids, the adrenal cortex is also able to hydroxylate steroids of both the C_{19} and C_{21} series at the 6 α -, 6 β - and 19-positions^{2,3}. Hydroxylations at C-6 are also known to occur in rat liver, and the guinea-pig adrenal converts cortisol to 2 α -hydroxycortisol²³. Urinary steroids (both C_{19} and C_{21}) having 16 α -hydroxy groups have also been isolated²⁴, and hog adrenal tissue is able to carry out hydroxylations at this position²⁵.

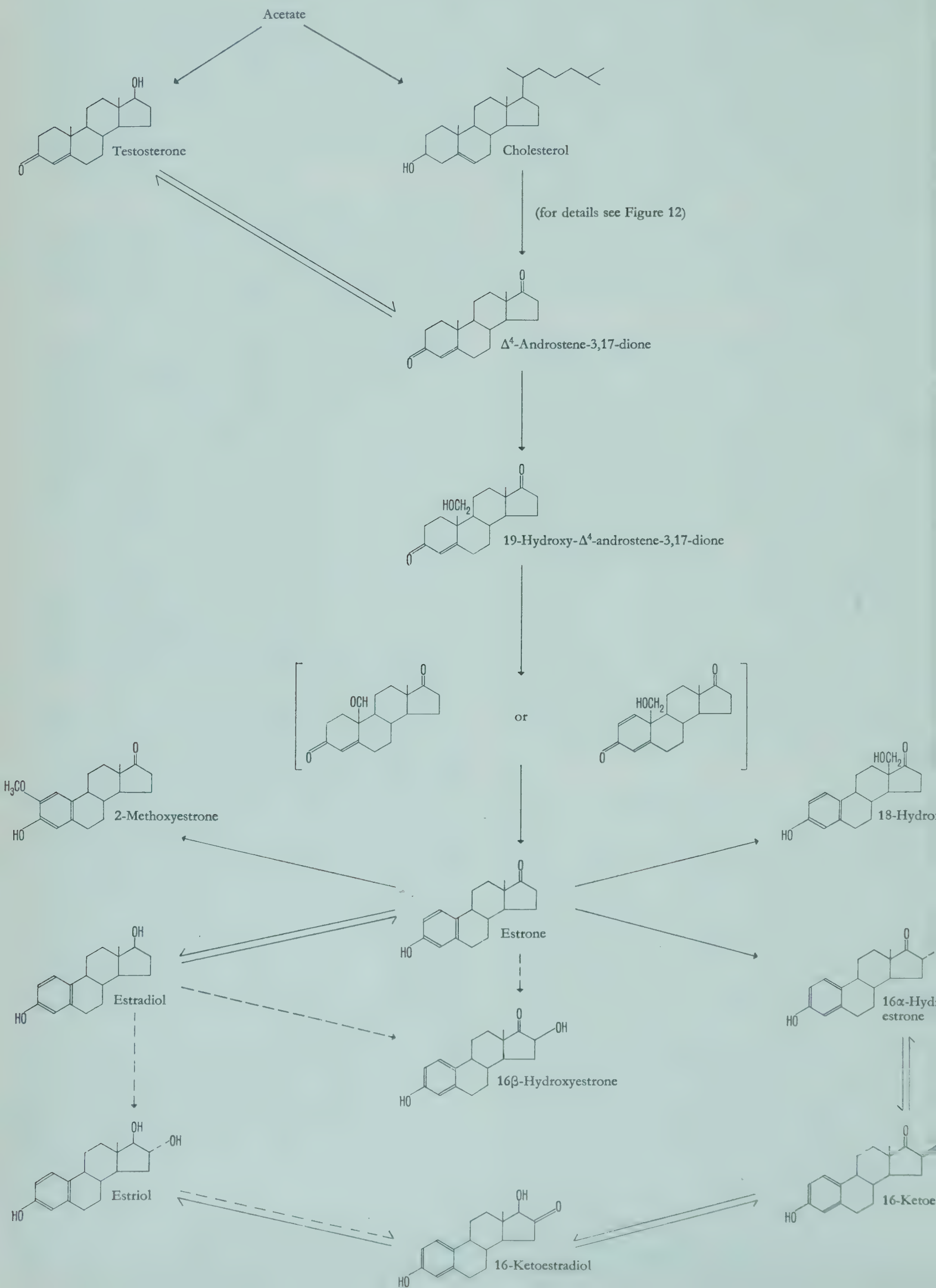
Reduction. In general, the body tends to eliminate steroid hormones in the form of metabolites in which the Δ^4 -3-keto system of ring A (see Figure 12) is totally reduced. Theoretically, this reduction may lead to products having either 3 α - or 3 β -hydroxy groups and the hydrogen atom at C-5 in either the 5 α - or 5 β -configuration. In practice, almost all reduced metabolites excreted by man are of the 3 α -hydroxy-5 β -(C_{21} :pregnane; C_{19} :etiocholan) series. Minor quantities of steroids of the 3 α -hydroxy-5 α -(C_{21} :allopregnane; C_{19} :androsterone) series are also excreted. Metabolism of steroid hormones by tissues of other species, in particular rat liver (*in vitro*) yields predominantly (but not exclusively) reduced products of the 5 α -series²⁶ having both 3 α - and 3 β -hydroxy groups. Reduction of the Δ^4 -3-keto moiety apparently proceeds in stepwise fashion, the Δ^4 -bond being reduced first²⁷.

Conversion of the 20-keto group to a 20-hydroxy group is a further important catabolic reduction of the C_{21} hormones and also follows a course in most *in vitro* tissue preparations²⁸ sterically different from that found in man²⁰. The product *in vitro* is generally a 20 β -hydroxy derivative; that excreted by man is almost exclusively a 20 α -hydroxy derivative.

Conjugation and excretion. The steroid excretion products of the urine are present largely in the form of conjugates²⁰ with glucuronic acid or with sulfate. The majority of the C_{21} metabolites are excreted as β -glucuronides. Dehydroepiandrosterone and androsterone are present in the urine to a major extent as sulfate conjugates. Cortisone and cortisol are apparently excreted in the urine largely in the free form. There is evidence that glucuronide formation in the liver is a general feature of steroid metabolism²⁹.

1) NOBLE, R. L., in PINCUS and THIMANN (Eds.), *The Hormones*, vol. III, New York, 1955, page 685. 2) DORFMAN, R. I., in PINCUS and THIMANN (Eds.), *The Hormones*, vol. III, New York, 1955, page 589. 3) HAYANO et al., *Recent Progr. Hormone Res.*, 12, 79 (1956). 4) HEARD et al., *Recent Progr. Hormone*

Fig. 13 Synthesis and metabolism of estrogens



Res. 12, 45 (1956). 5) DORFMAN, R. I., *Ciba Foundation Colloquia on Endocrinology*, 8, 112 (1955); CORNFORTH et al., *Proc. chem. Soc. Lond.*, 1958, 112. 6) KAHNT et al., *Experientia (Basel)*, 11, 446 (1955). 7) KAHNT et al., *Helv. chim. Acta*, 38, 1237 (1955). 8) KASS et al., *Proc. Soc. exp. Biol.*, 85, 583 (1954). 9) ROSENFIELD and BASCOM, *Endocrinology*, 59, 497 (1956). 10) SIMPSON et al., *Experientia (Basel)*, 10, 132 (1954). 11) DESAULLES et al., *Schweiz. med. Wschr.*, 83, 1088 (1953). 12) SCHULER et al., *Experientia (Basel)*, 10, 142 (1954). 13) GROSS and GYSEL, *Acta endocr. (Kbh.)*, 15, 199 (1954). 14) MACH et al., *Schweiz. med. Wschr.*, 84, 407 (1954). 15) EALES and LINDER, *Quart. J. Med.*, 25, 539 (1956). 16) SKANSE and HÖKFELT, *Acta endocr. (Kbh.)*, 28, 29 (1958). 17) LUETSCHER, J. A., *Recent Progr. Hormone Res.*, 12, 175 (1956). 18) FARRELL, G., *Recent Progr. Hormone Res.*, 12, 192 (1956). 19) AXELRAD et al., *Brit. med. J.*, 1, 196 (1955). 20) ROBERTS and SZEGO, *Ann. Rev. Biochem.*, 24, 543 (1955). 21) SLAUNWHITE and SAMUELS, *J. biol. Chem.*, 220, 341 (1956); LYNN, W. S., *Fed. Proc.*, 15, 305 (1956). 22) SOLOMON et al., *J. Amer. chem. Soc.*, 78, 5453 (1956). 23) BURSTEIN, S., *J. Amer. chem. Soc.*, 78, 1769 (1956). 24) LIEBERMAN et al., *J. biol. Chem.*, 204, 491 (1953). 25) RAO and HEARD, *Arch. Biochem. Biophys.*, 66, 504 (1957). 26) FORCHIELLI and DORFMAN, *J. biol. Chem.*, 223, 443 (1956); BURSTEIN et al., *Endocrinology*, 56, 267 (1955). 27) TOMKINS, G. M., *J. biol. Chem.*, 225, 13 (1957). 28) CASPI and HECHTER, *Arch. Biochem. Biophys.*, 61, 299 (1956); DE COURCY and SCHNEIDER, *J. biol. Chem.*, 223, 865 (1956). 29) SIE and FISHMAN, *J. biol. Chem.*, 225, 453 (1957).

Synthesis and metabolism of estrogens

The principal estrogenic steroids of the human are estrone, estradiol and estriol. They are C_{18} compounds in which ring A is phenolic. The major sites of synthesis are the ovary and placenta, although synthesis also takes place in the testes and adrenal cortex. Less is known of the pathways of synthesis of estrogens than of any other group of steroid hormones^{1,2}. Present knowledge is derived from urinary excretion studies which have been carried out principally with humans and horses, and from studies *in vitro* carried out with various mammalian tissues. It is outlined in Figure 13 (page 506).

Cholesterol has been shown to give rise to androgens, and androgens have in turn been shown to be converted into estrogens^{2,3}. In pregnancy a conversion of cholesterol to estrogens has been found to occur⁹. The estrogens are probably derived from androgens via 19-hydroxy- Δ^4 -androstenedione, since conversion of Δ^4 -androstenedione to the 19-hydroxy derivative has been demonstrated and it has been observed that estrone is formed more rapidly from the 19-hydroxy compound than from Δ^4 -androstenedione itself. By analogy with the chemical reactivity of other compounds of similar structure, the aromatization of the 19-hydroxy compound is thought to proceed either via 19-aldo- Δ^4 -androstenedione or 19-hydroxy- $\Delta^{1,4}$ -androstadienedione, both of which could lose formaldehyde to give estrone.

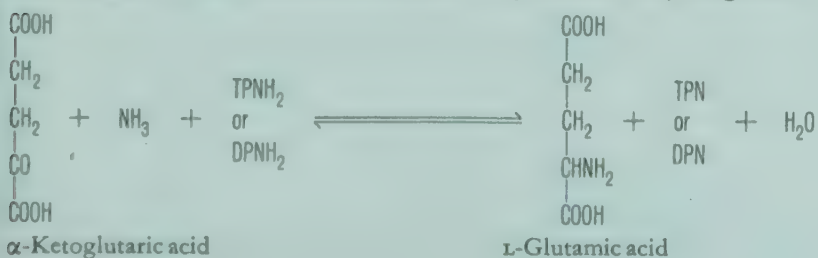
16-Ketoestrone and 16-ketoestradiol are probable intermediates in the conversion of estrone to estriol⁴. 16-Ketoestrone is formed from estrone *in vivo*⁴ and is converted to 16-ketoestradiol which in turn gives rise to estriol⁵. Two 16-hydroxyestrones have been isolated from pregnancy urine⁶ and some estrone is excreted as its 18-hydroxy derivative, presumably formed in the adrenal⁷. 2-Methoxyestrone has been identified in urine and is presumably also a normal metabolite⁸.

A direct conversion of estradiol to estriol has not been observed and remains hypothetical. For further discussion of estrogen metabolism see pages 201–202.

1) DORFMAN, R. I., in PINCUS and THIMANN (Eds.), *The Hormones*, vol. III, New York, 1955, page 593. 2) HEARD et al., *Recent Progr. Hormone Res.*, 12, 45 (1956). 3) BAGGETT et al., *J. biol. Chem.*, 221, 931 (1956). 4) SLAUNWHITE and SANDBERG, *Arch. Biochem. Biophys.*, 63, 478 (1956). 5) LEVITZ et al., *J. biol. Chem.*, 222, 981 (1956). 6) MARRIAN et al., *Biochem. J.*, 66, 60 (1957); LAYNE and MARRIAN, *Nature*, 182, 50 (1958); BROWN et al., *Nature*, 182, 50 (1958). 7) LOKE et al., *Biochim. biophys. Acta*, 28, 214 (1958). 8) KRAYCHY and GALLAGHER, *J. biol. Chem.*, 229, 519 (1957). 9) WERBIN et al., *J. Amer. chem. Soc.*, 79, 1012 (1957).

Formation of glutamic acid

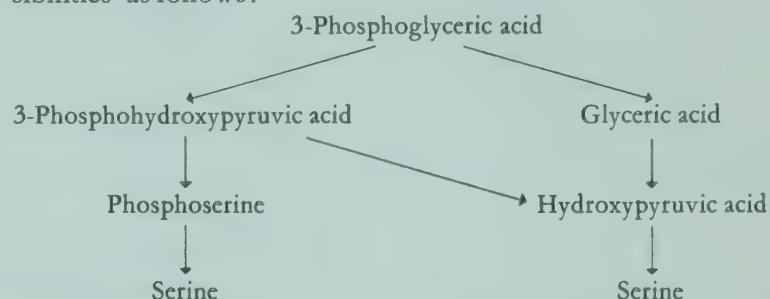
Glutamic acid is readily synthesized in liver and other animal tissues when α -ketoglutarate, ammonia and reduced DPN or TPN are available. The reaction is catalyzed by glutamic dehydrogenase:



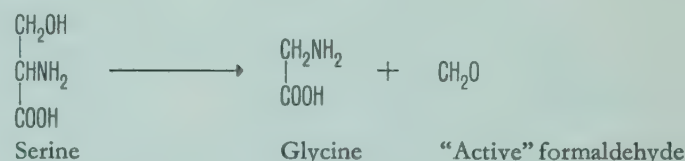
Glutamic acid is the only amino acid in animal tissues which can be directly synthesized from ammonia and the corresponding carbon skeleton (supplied in the form of the α -ketonic acid). All other nonessential amino acids are formed from the corresponding α -ketonic acids by transamination with glutamate. The reductive amination of α -ketoglutarate is thus the most important ammonia-binding reaction in the animal body.

Formation of serine and glycine from carbohydrate

Serine can be formed from glucose via phosphoglyceric acid. It is not certain at what stage the phosphate is removed from the ester link and the evidence is in accordance with several possibilities¹ as follows:



That glycine arises from serine in the mammalian body is firmly established:

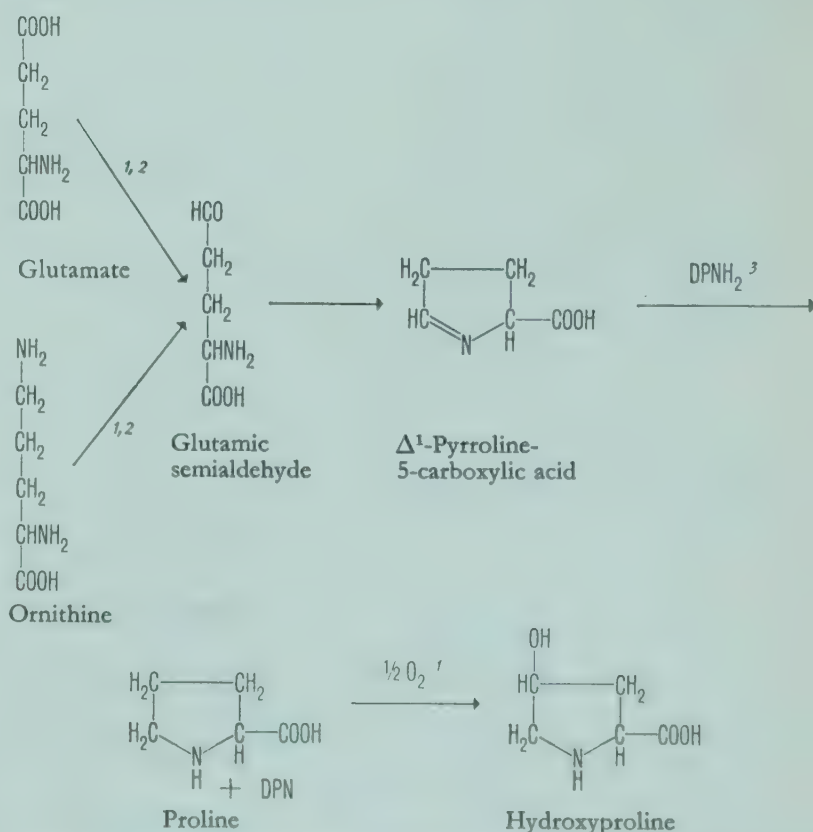


The enzymic mechanisms, however, are unknown².

1) KORKES, S., *Ann. Rev. Biochem.*, 25, 732 (1956). 2) ARNSTEIN, H. R. V., *Advanc. Protein Chem.*, 9, 1 (1954) (especially page 36).

Formation of proline and hydroxyproline

These amino acids are assumed to be formed from ornithine or glutamic acid via glutamic semialdehyde according to the following sequence of reactions:



1) STETTEN, M. R., in McELROY and GLASS (Eds.), *A Symposium on Amino Acid Metabolism*, Baltimore, 1955, page 277; VOGEL, H. J., *ibid.*, page 335. 2) STRECKER and MELA, *Biochim. biophys. Acta*, 17, 580 (1955). 3) YURA and VOGEL, *Biochim. biophys. Acta*, 17, 582 (1955); SMITH and GREENBERG, *Nature*, 177, 1130 (1956).

Table 20 Formation of basic cell constituents and metabolites from amino acids
This list is not comprehensive; for carbohydrate synthesis from amino acids see page 514

Amino acid serving as starting material	Product formed	Pathway of formation	Physiological function
Glycine	Purine bases	See page 509	Constituent of nucleic acids and nucleotides
	Porphyrins	See page 511	Constituent of hemoglobin and cytochromes
	Creatine	See page 511	Precursor of creatine phosphate, an energy store in muscle and other tissues
	Glutathione	See page 512	Prosthetic group of glyoxalase triosephosphate dehydrogenase and probably other enzymes
	Hippuric acid and related compounds	See page 519	Detoxication product of benzoic acid
	Bile acids	See page 512	Required for digestion of fats
Serine	Ethanolamine	Decarboxylation (see Table 6, page 477)	Constituent of phospholipids
	Choline	Methylation of ethanolamine, methionine acting as a methyl group donor	Constituent of phospholipids
	Acetylcholine	Acetylation of choline by acetyl-coenzyme A ¹	Transmitter substance at nerve endings
Cysteine	Taurine	See page 512	Constituent of bile acids
	Glutathione	See page 512	See above under Glycine
Glutamic acid	Glutamine	From glutamic acid and ammonia in the presence of ATP ²	Cell constituent. Intermediate carrier of amino groups in aminations and amidations
	γ-Aminobutyric acid	Decarboxylation (see Table 6, page 477)	Cell constituent, especially of brain
	Glutathione	See page 512	See above under Glycine
	Proline	See page 507	Protein constituent
	Hydroxyproline	See page 507	Protein constituent
Arginine	Creatine	See page 511	See above under Glycine
Methionine	Creatine	See page 511	See above under Glycine
	Choline	Decarboxylation (see Table 6, page 477)	See above under Serine
Histidine	Histamine	See page 477	Transmitter substance at nerve endings
Aspartic acid	Pyrimidine bases	See page 513	Constituent of nucleic acids and nucleotides
	β-Alanine	Probably by α-decarboxylation	Constituent of special peptides (anserine, carnosine, pantothenic acid)
Tyrosine	Adrenaline	See page 513	Hormone
	Noradrenaline	See page 513	Hormone and transmitter substance at nerve endings
	Thyroxine	See page 514	Hormone
	Melanins	See page 514	General pigments of hair and skin
Tryptophan	5-Hydroxytryptamine (serotonine)	See page 514	Transmitter substance at nerve endings
	Nicotinic acid	See page 482	Constituent of pyridine nucleotides
Glucogenic amino acids	Carbohydrates	See page 515	

1) KORKES et al., *J. biol. Chem.*, **198**, 215 (1952). 2) ELLIOTT, W. H., *J. biol. Chem.*, **201**, 661 (1953).

2. Formation of basic cell constituents and metabolites from amino acids

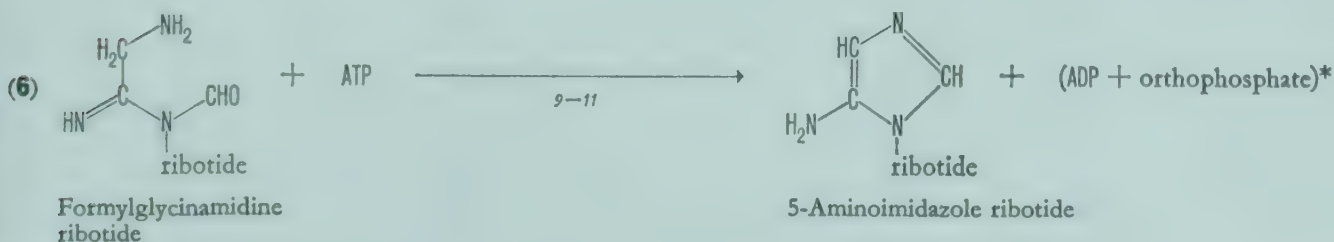
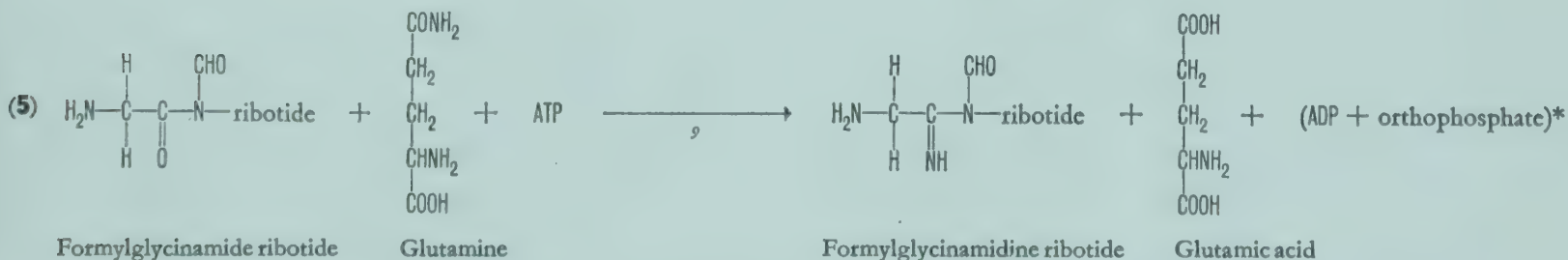
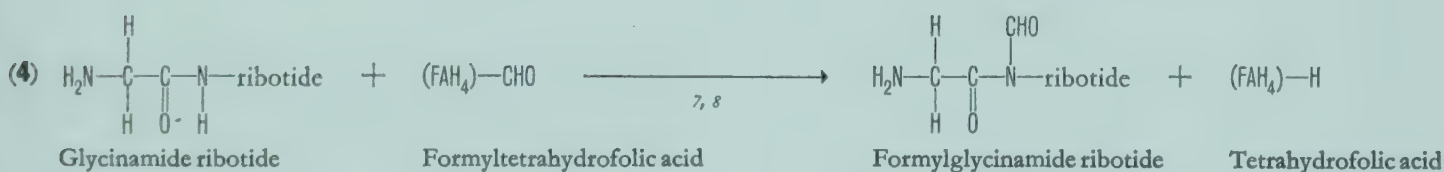
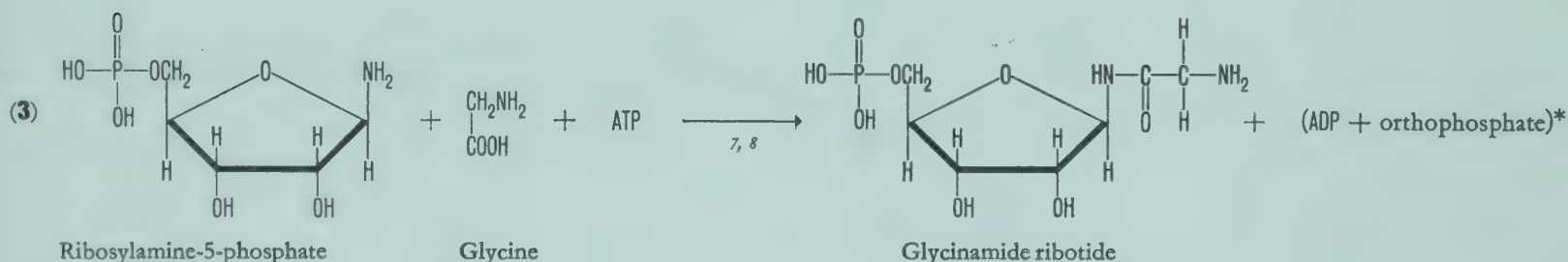
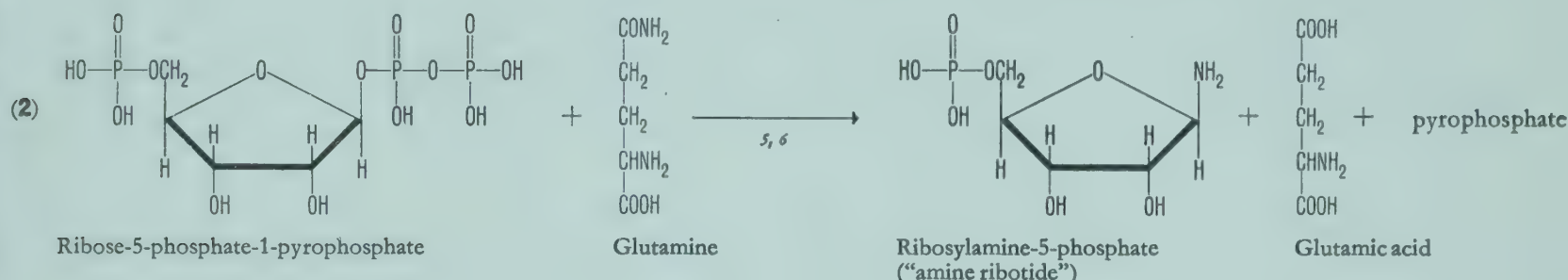
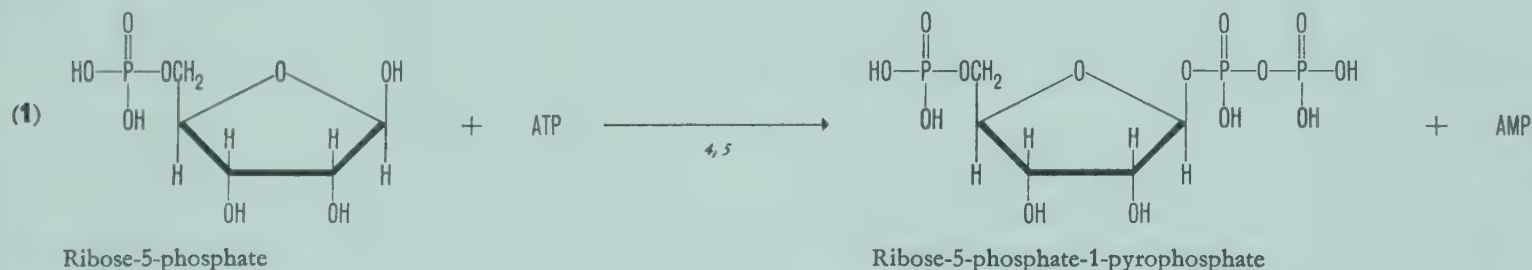
The principal products, their pathways of formation and their physiological functions are summarized in Table 20 on page 508.

Formation of purines

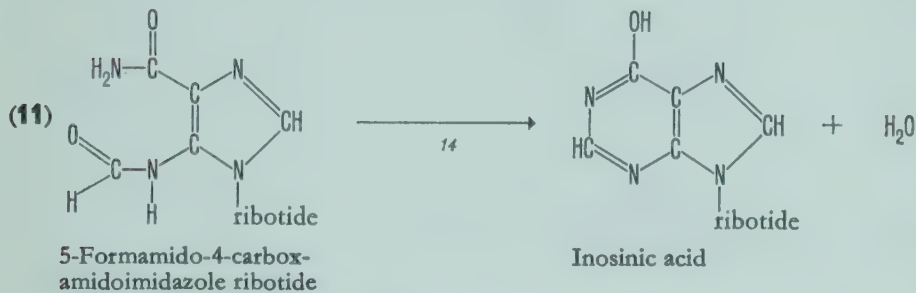
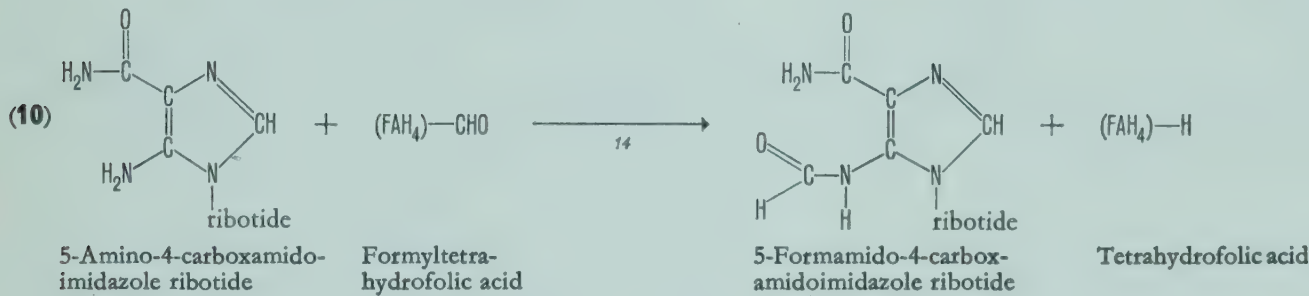
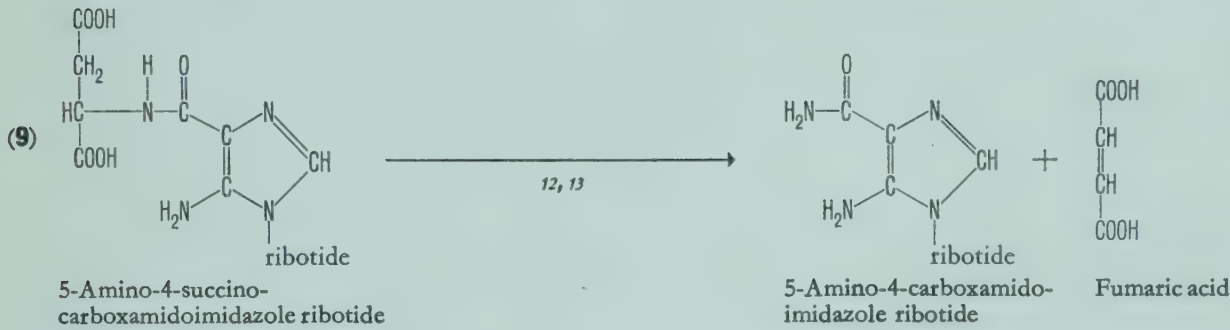
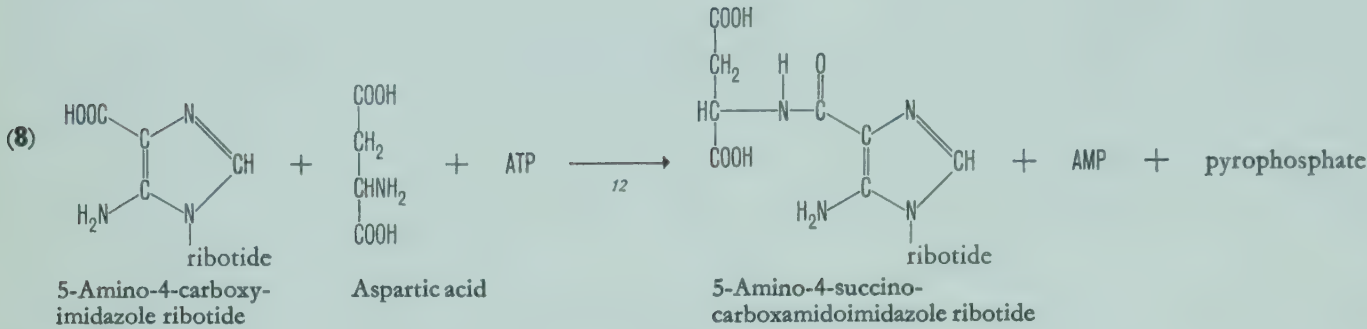
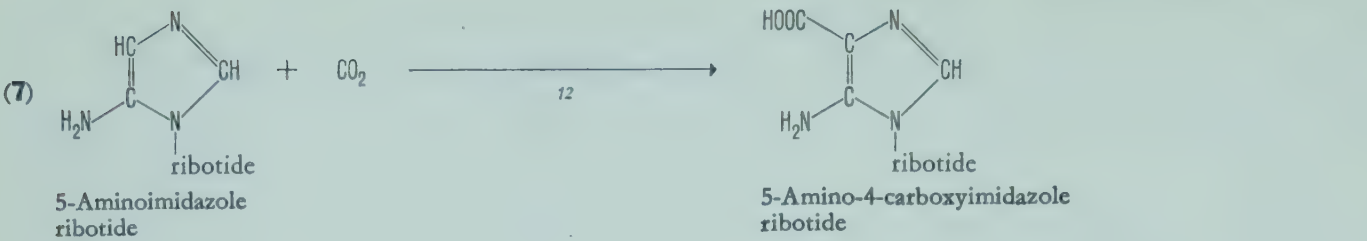
Knowledge of the pathway shown below (pages 509–511) is derived mainly from work done on pigeon liver. There is, however, no reason to doubt that the same pathway occurs in mammals. The purine skeleton is built up on the nitrogen atom of ribosylamine-5-phosphate. The substrates utilized in this process include glutamine, glycine, aspartic acid, carbon dioxide, and a

one-carbon fragment equivalent to formaldehyde which is supplied in the form of formyltetrahydrofolic acid¹. The first purine derivative to be formed is inosinic acid (reactions 1–11). This is then converted into adenylic acid (reactions 12 and 13) or into xanthidylic acid (reaction 14) and guanylic acid (reaction 15). Only adenine is utilized directly when the naturally occurring purines are ingested as the free bases. It is probably converted into AMP by a reaction similar to the conversion of orotic acid to orotidylic acid (see page 513)². Other purine bases such as guanine, hypoxanthine and xanthine are utilized to a very small extent or not at all³.

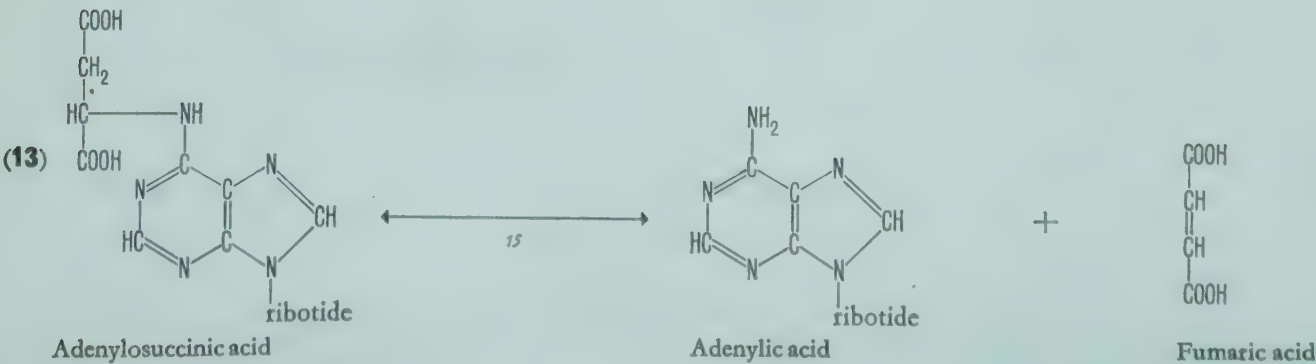
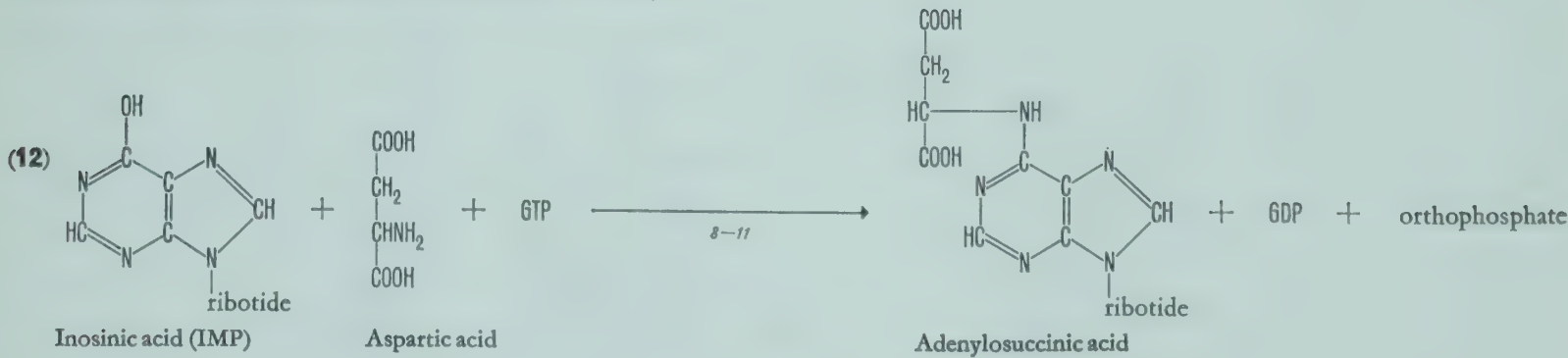
Formation of inosinic acid (IMP)



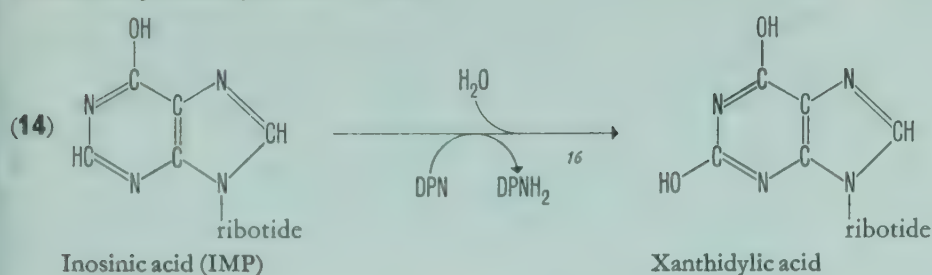
* The nature of the products given in brackets is not established with certainty.



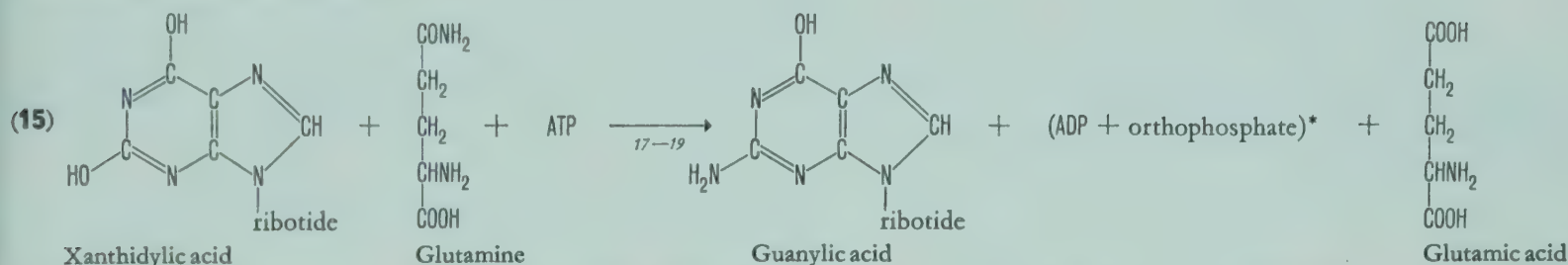
Formation of adenylic acid (adenosine monophosphate, AMP)



Formation of xanthidylic acid (XMP)



Formation of guanylic acid (GMP)



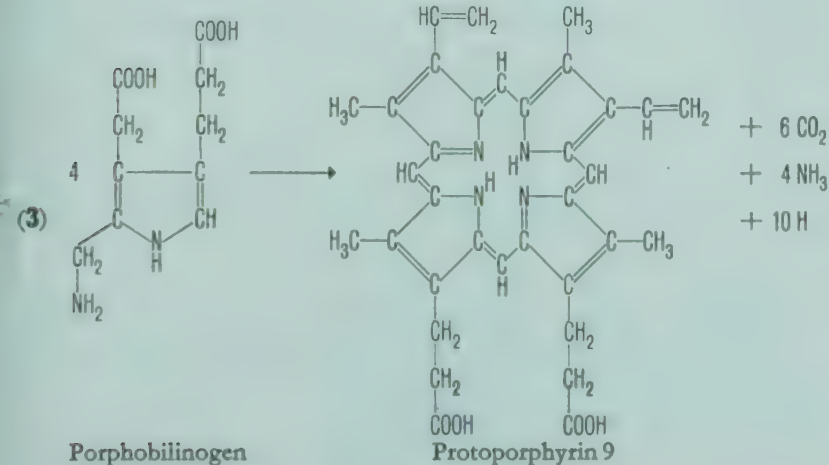
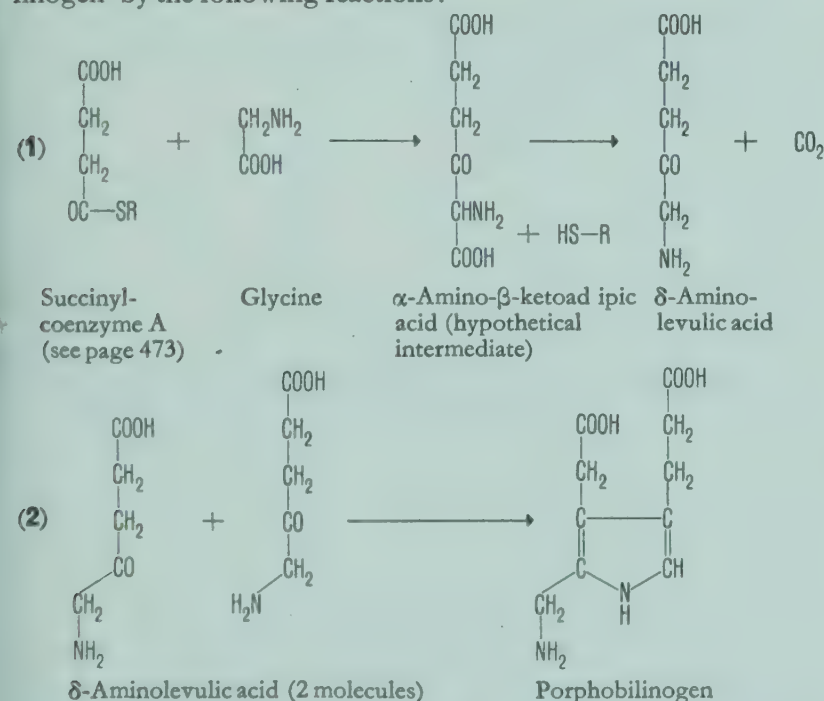
* The nature of these products is not established with certainty.

1) CARTER, C. E., *Ann. Rev. Biochem.*, **25**, 123 (1956). 2) KORNBERG et al., *J. biol. Chem.*, **215**, 417 (1955). 3) CHRISTMAN, A. A., *Physiol. Rev.*, **32**, 303 (1952). 4) KORNBERG et al., *J. biol. Chem.*, **215**, 389 (1955). 5) GOLDTHWAIT et al., *Biochim. biophys. Acta*, **18**, 148 (1955). 6) GOLDTHWAIT, D. A., *J. biol. Chem.*, **222**, 1051 (1956). 7) GOLDTHWAIT et al., *J. biol. Chem.*, **221**, 569 (1956); WARREN and BUCHANAN, *J. biol. Chem.*, **229**, 613 (1957). 8) HARTMAN et al., *J. biol. Chem.*, **221**, 1057 (1956). 9) LEVENBERG and BUCHANAN, *J. biol. Chem.*, **224**, 1005, 1019 (1957); MELNICK and BUCHANAN, *J. biol. Chem.*, **225**, 157 (1957).

10) GOLDTHWAIT et al., in McELROY and GLASS (Eds.), *A Symposium on Amino Acid Metabolism*, Baltimore, 1955, page 765. 11) BUCHANAN et al., in McELROY and GLASS (Eds.), *A Symposium on Amino Acid Metabolism*, Baltimore, 1955, page 743. 12) LUKENS, L. N., *Abstr. Amer. chem. Soc. 131st Meeting*, 1957, page 14C. 13) MILLER et al., *J. Amer. chem. Soc.*, **79**, 1513 (1957). 14) FLAKS et al., *J. biol. Chem.*, **229**, 603 (1957). 15) LIEBERMAN, I., *J. biol. Chem.*, **223**, 327 (1956). 16) CARTER and COHEN, *J. biol. Chem.*, **222**, 17 (1956). 17) ABRAMS and BENTLEY, *Arch. Biochem. Biophys.*, **58**, 109 (1955). 18) LAGERKVIST, U., *Acta chem. scand.*, **9**, 1028 (1955). 19) GEHRING and MAGASANIK, *J. Amer. chem. Soc.*, **77**, 4685 (1955).

Formation of porphyrins

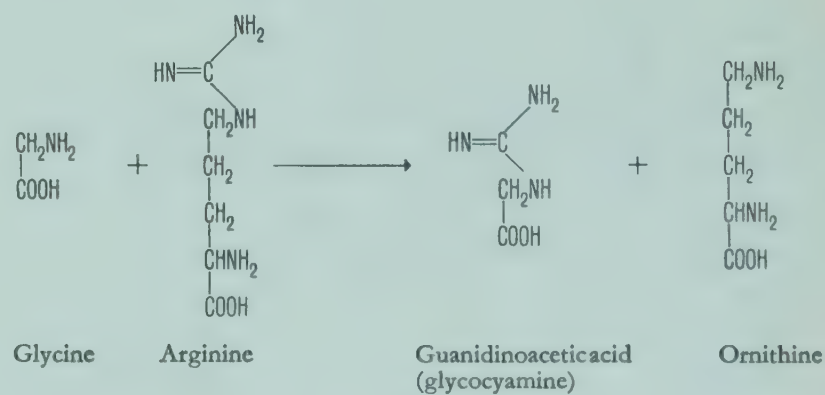
Eight of the carbon atoms of the porphyrin molecule are derived from the α -carbon atom of glycine; the remaining twenty-six carbon atoms are derived from succinic acid. The four nitrogen atoms of the molecule are derived from the amino group of glycine¹. The formation of this complex molecule has been demonstrated to proceed via δ -aminolevulinic acid and porphobilinogen² by the following reactions:



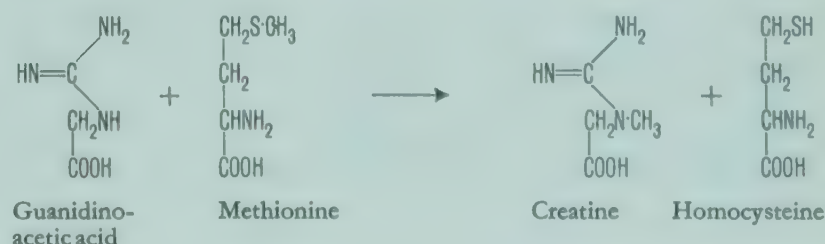
1) SHEMIN, D., in McELROY and GLASS (Eds.), *A Symposium on Amino Acid Metabolism*, Baltimore, 1955, page 727; SHEMIN, D., *Ergebn. Physiol.*, **49**, 299 (1957). 2) BERLIN et al., *Biochem. J.*, **64**, 80 (1956); WRISTON et al., *J. biol. Chem.*, **215**, 603 (1955); FALK et al., *Nature*, **172**, 292 (1953); NEMETH et al., *J. biol. Chem.*, **229**, 415 (1957); GIBSON et al., *Biochem. J.*, **68**, 17P (1958).

Formation of creatine from glycine, arginine and methionine¹

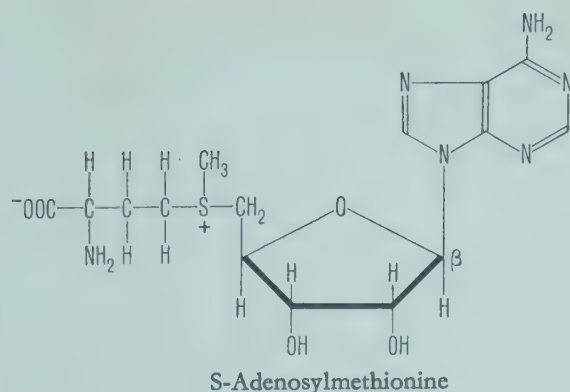
Creatine (which in the form of creatine phosphate serves as a store of "phosphate bond energy") is formed by two transfer reactions. The basic skeleton of creatine is provided by glycine. In the first transfer reaction the group $\text{HN}=\text{C}-\text{NH}_2$ is transferred from arginine to glycine:



In the second reaction the methyl group of methionine is transferred to the guanidinoacetic acid formed in the first reaction:

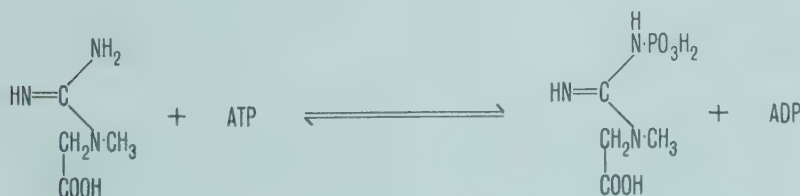


Methionine does not react as the free amino acid but as the S-adenosyl derivative, formed from ATP and methionine²:



Homocysteine appears likewise as the adenosyl derivative in the transmethylation reaction formulated above.³

Creatine interacts reversibly with ATP, especially in muscle, to form creatine phosphate:

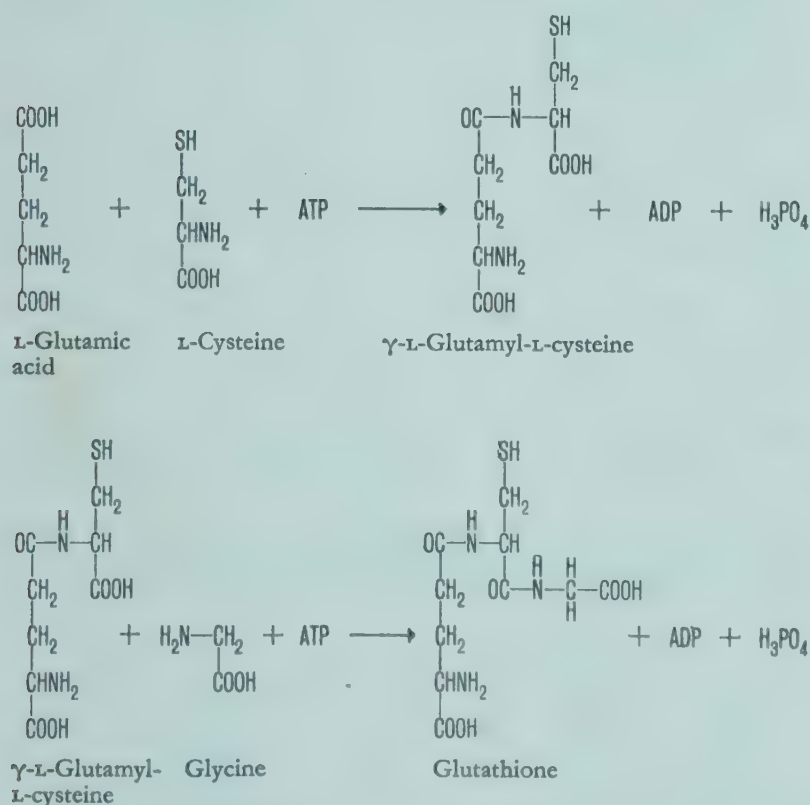


The reaction proceeds from left to right in resting muscle, and from right to left during prolonged contractions, regenerating ATP spent as an energy source in the process of contraction.

- 1) For a review see ARNSTEIN, H. R. V., *Advanc. Protein Chem.*, **9**, 1 (1954).
 2) CANTONI, G. L., *J. biol. Chem.*, **204**, 403 (1953); CANTONI and SCARANO, *J. Amer. chem. Soc.*, **76**, 4744 (1954); CANTONI and VIGNOS, *J. biol. Chem.*, **209**, 647 (1954). 3) CANTONI and SCARANO, *J. Amer. chem. Soc.*, **76**, 4744 (1954).

Formation of glutathione

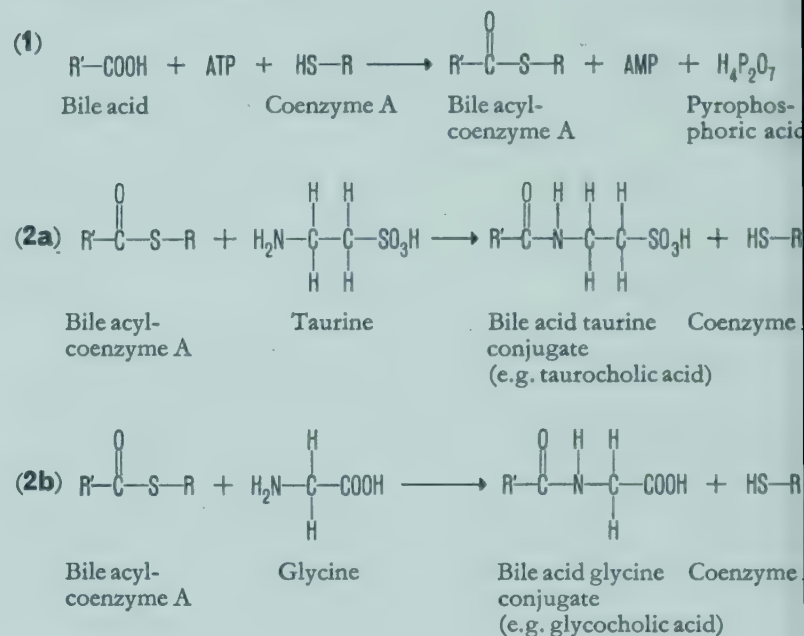
Glutathione is formed in two main steps which have been demonstrated to occur in the liver. The first of these involves the formation of the dipeptide γ -L-glutamyl-L-cysteine from glutamic acid, cysteine and ATP¹. This is followed by the formation of glutathione itself from γ -L-glutamyl-L-cysteine, glycine and ATP².



- 1) MANDELES and BLOCH, *J. biol. Chem.*, **214**, 639 (1955). 2) SNOKE, J. E., *J. biol. Chem.*, **213**, 813 (1955).

Formation of bile acid conjugates¹

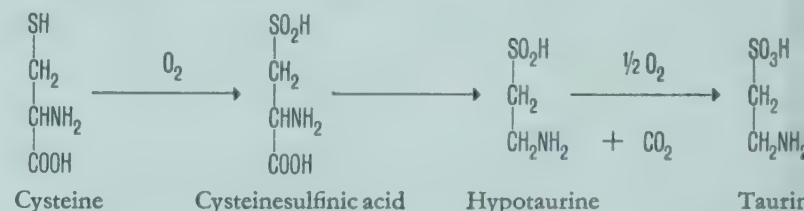
Bile acids such as cholic and desoxycholic acids are excreted into the intestine in the form of glycine or taurine conjugates. The major factors controlling the ratios of glycine and taurine conjugates appear to be the availability of taurine. The specificity and activity of the enzyme systems are such as to favor the formation of taurine conjugates². The reactions require the presence of coenzyme A and ATP, and presumably proceed by a mechanism similar to that involved in the activation of acetate (page 474) and aromatic acids (page 519)³.



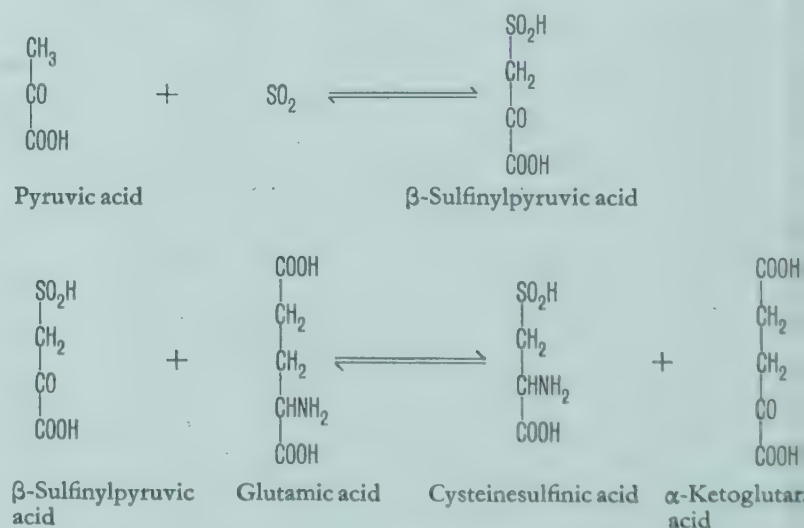
- 1) BERGSTROM and BERGSTROM, *Ann. Rev. Biochem.*, **25**, 187 (1956). 2) BREMER, J., *Acta chem. scand.*, **9**, 268 (1955). 3) BREMER, J., *Acta chem. scand.*, **9**, 1036 (1955); ELLIOTT, W. H., *Biochem. J.*, **62**, 427, 433 (1955); **65**, 315 (1957).

Formation of taurine

Taurine is formed from cysteine in the liver and possibly in other organs. The pathway in mammalian tissues is via cysteinesulfinic acid and hypotaurine¹:



Cysteinesulfinic acid may also be formed from pyruvic acid, sulfur dioxide and glutamic acid by the following reactions²:

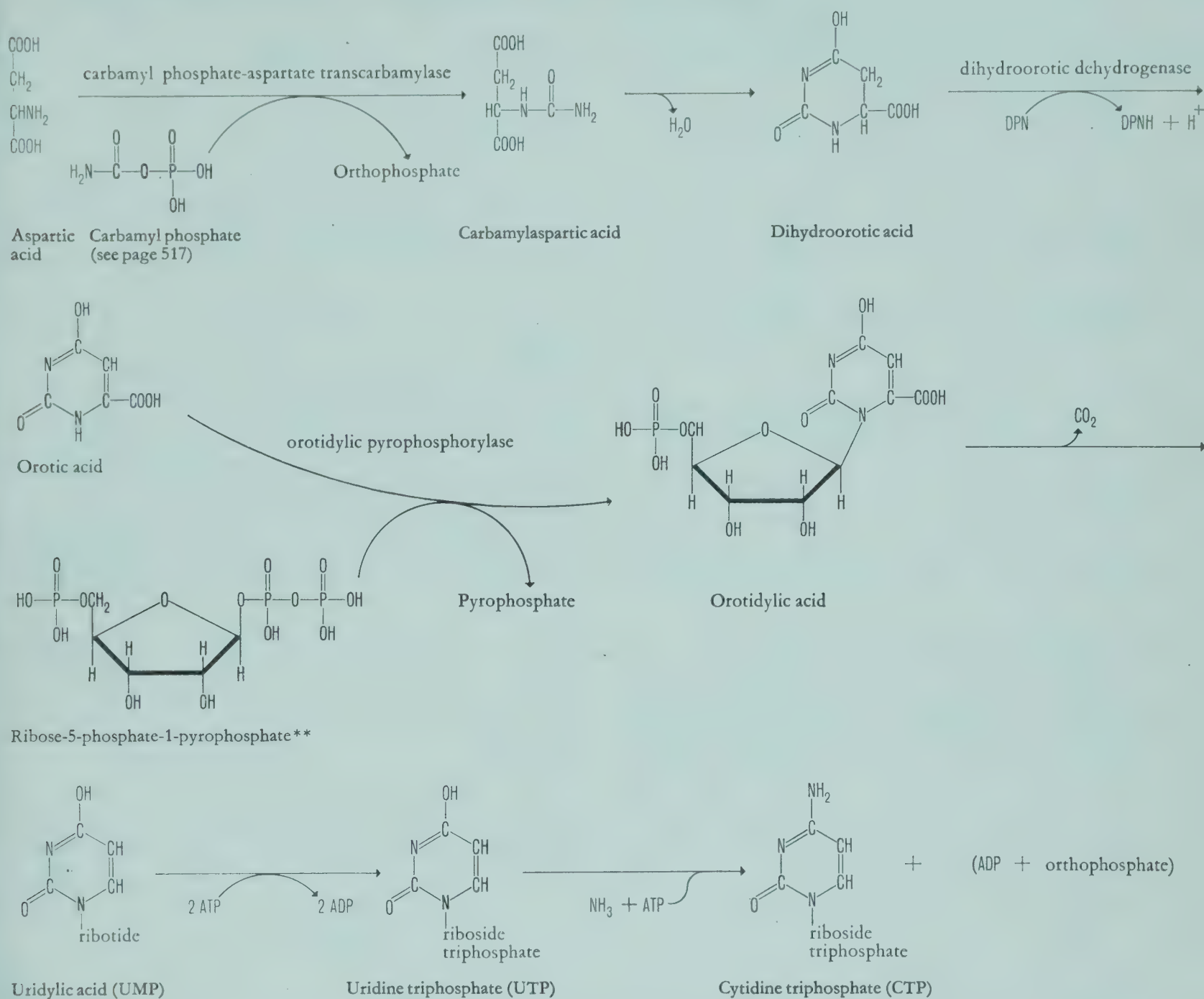


- 1) AWAPARA and WINGO, *J. biol. Chem.*, **203**, 189 (1953); CAVALLINI et al., *J. biol. Chem.*, **216**, 577 (1955); HOPE, B. D., *Biochem. J.*, **59**, 497 (1955); BERGERET et al., *Biochim. biophys. Acta*, **17**, 128 (1955); CHAPEVILLE and FROMAGEOT, *Biochim. biophys. Acta*, **17**, 275 (1955). 2) CHAPEVILLE and FROMAGEOT, *Biochim. biophys. Acta*, **14**, 415 (1954).

Formation of pyrimidines

The starting materials of pyrimidine synthesis are aspartic acid and carbamyl phosphate. The pathway shown below occurs in mammals¹ and bacteria². Orotic acid is the first complete pyrimidine

to be formed. This is converted to orotidylic acid (OMP)³ and then to uridylic acid (UMP), cytidylic acid⁴ and thymidylic acid* (TMP). The manner in which the latter is formed has not been determined.



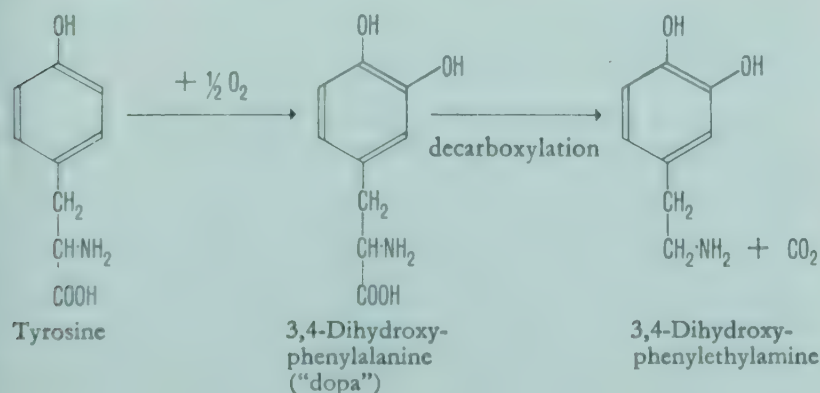
* Strictly speaking, this compound should be termed desoxythymidylic acid (DTMP) since it contains desoxyribose.

** This compound is formed by reaction (1), page 509.

1) CARTER, C. E., *Ann. Rev. Biochem.*, **25**, 123 (1956); LOWENSTEIN and COHEN, *J. biol. Chem.*, **220**, 57 (1956); COOPER et al., *J. biol. Chem.*, **216**, 37 (1955). 2) LIEBERMAN and KORNBERG, *J. biol. Chem.*, **207**, 911 (1954). 3) LIEBERMAN et al., *J. biol. Chem.*, **215**, 403 (1955). 4) LIEBERMAN, I., *J. biol. Chem.*, **222**, 765 (1956).

Formation of adrenaline and noradrenaline from tyrosine

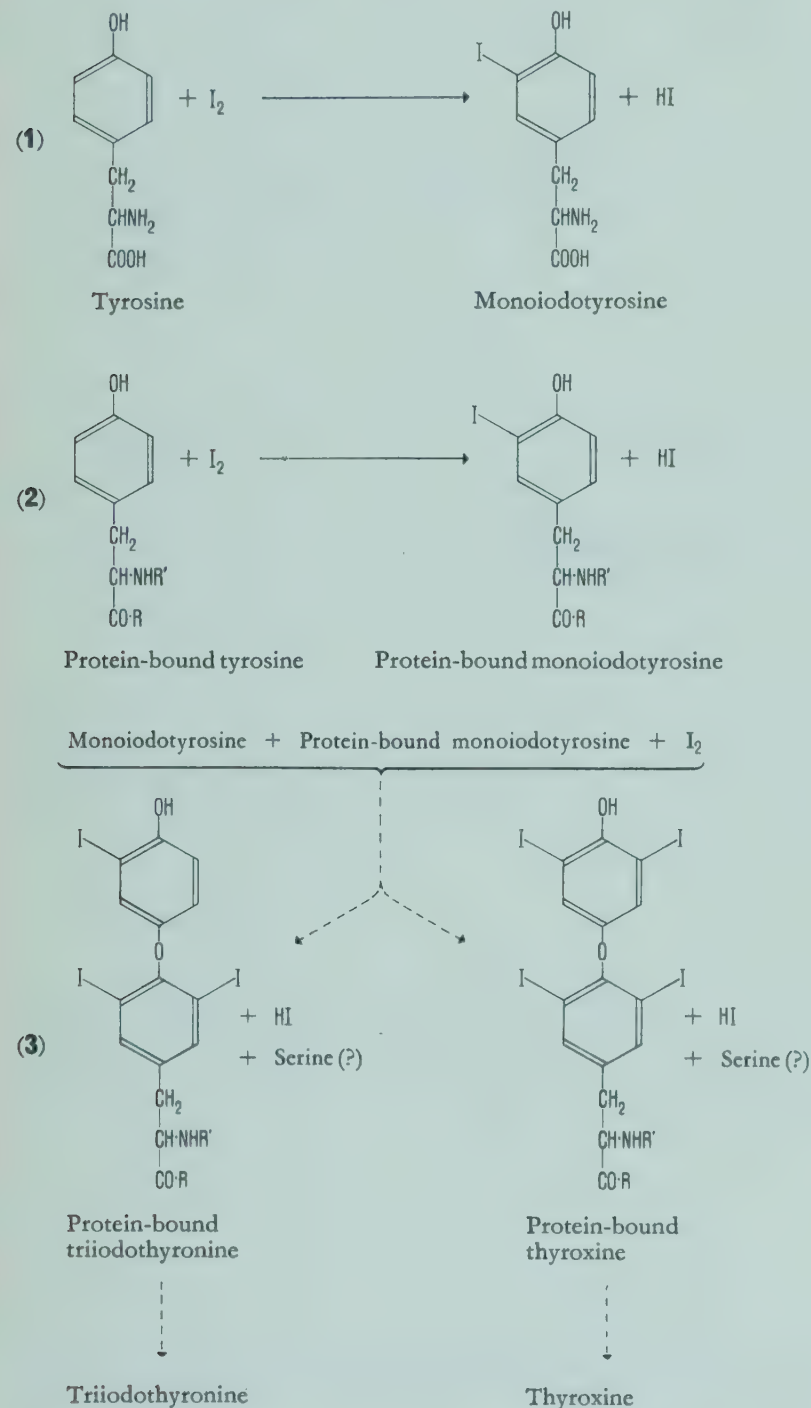
Isotopic evidence has proved conclusively that adrenaline can be formed from phenylalanine and tyrosine, but the details of the intermediary reactions can only be tentatively formulated. The following is the most probable pathway¹:



1) For alternative pathways see DALGLIESH, C. E., *Advanc. Protein Chem.*, **10**, 65 (1955).

Formation of thyroid hormones¹

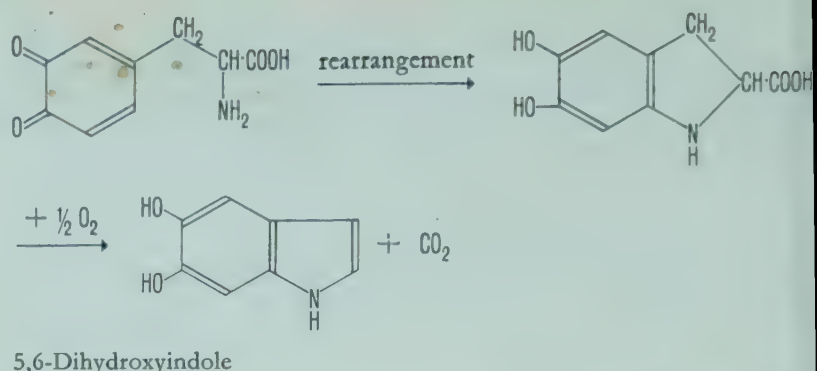
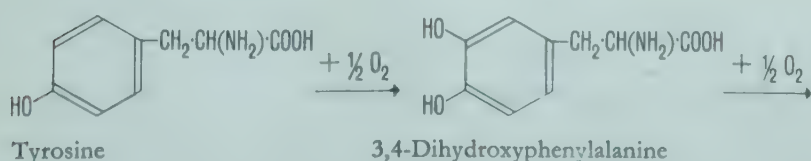
The thyroid gland has the capacity to concentrate iodide (I^-) from a blood level of about 1 μg per 100 ml to a gland level of about 10 μg per 100 g tissue. This concentration ratio may vary since it is influenced by a variety of factors such as the plasma iodide level. The incorporation of iodine into thyroid protein is a process the details of which are not yet known. It possibly occurs via free iodine (I_2) and involves the iodination of both free and protein-bound tyrosine²:



1) For a review see ROCHE and MICHEL, *Physiol. Rev.*, **35**, 583 (1955). 2) FAWCETT and KIRKWOOD, *J. biol. Chem.*, **209**, 249 (1954); TAUROG et al., *J. biol. Chem.*, **213**, 119 (1955).

Formation of melanin from tyrosine¹

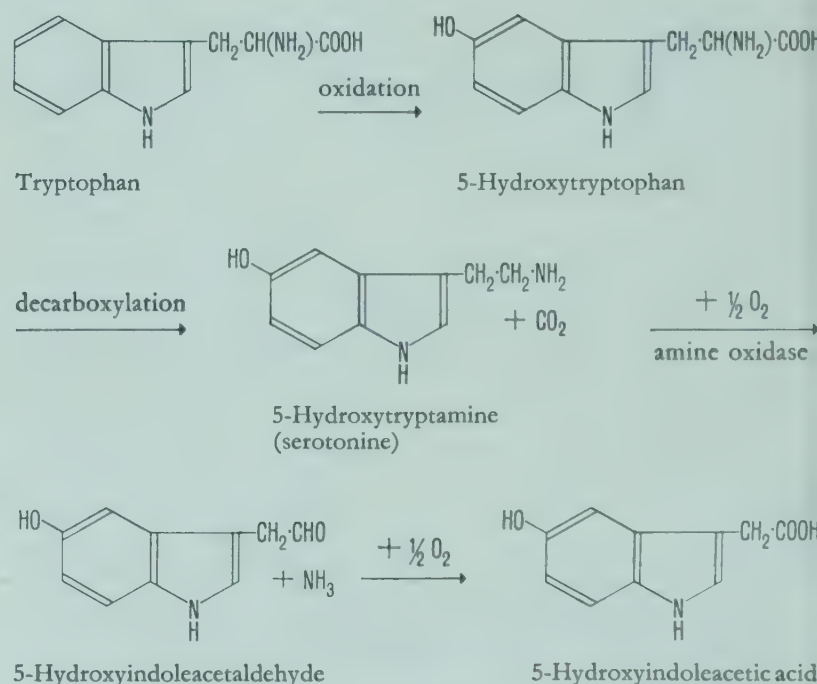
Melanin is the pigment of vertebrate skin, hair, feathers and eyes. It is a complex and nonhomogeneous substance. The chief basic unit is 5,6-dihydroxyindole which undergoes polymerization and in the polymerized form combines with protein. It is formed from tyrosine, probably by the following route (this route is blocked in albinism):



1) For a review see MASON, H. S., *Advanc. Enzymol.*, **16**, 163 (1955); DALGLIESH, C. E., *Advanc. Protein Chem.*, **10**, 65 (1955).

Formation and degradation of 5-hydroxytryptamine (serotonin)

5-Hydroxytryptamine (serotonin) is assumed to be a transmitter substance at nerve endings; it may play a role in hemostasis, in the control of renal activity, and has probably other functions¹. It is found in relatively high concentrations in thrombocytes and in the argentaffine cells of the intestinal wall. Its degradation product, 5-hydroxyindoleacetic acid, appears in the urine in abnormal quantities in cases of tumors of the argentaffine cells (argentaffinoma, malignant carcinoid)². 5-Hydroxytryptamine is assumed to be formed from tryptophan by the following reactions³:



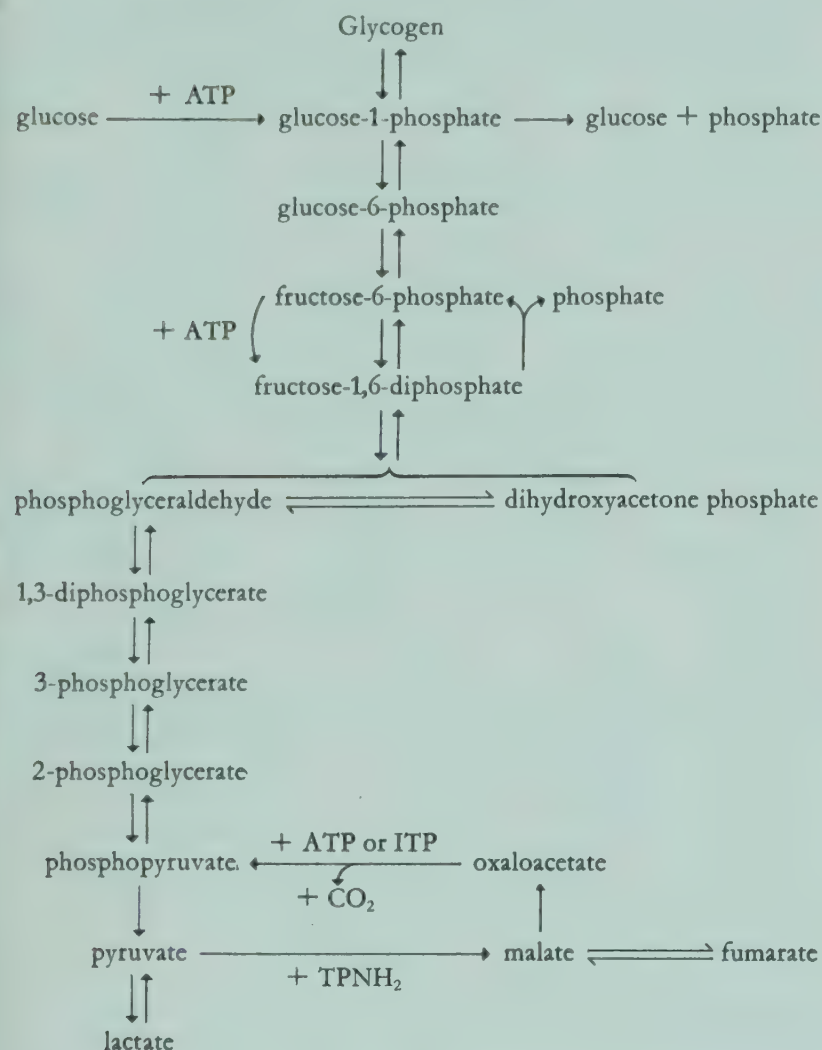
1) PAGE, I. H., *Physiol. Rev.*, **34**, 563 (1954); ERSPAMER, V., *Pharmacol. Rev.*, **6**, 425 (1954); SPECTOR and WILLOUGHBY, *Nature*, **179**, 318 (1957). 2) PAGE et al., *Lancet*, **1**, 198 (1955); PERNOW and WALDENSTRÖM, *Lancet*, **2**, 951 (1954). 3) UDENFRIEND et al., *J. Amer. chem. Soc.*, **75**, 501 (1953); DALGLIESH, C. E., *Advanc. Protein Chem.*, **10**, 103 (1955); DALGLIESH, C. E., *Biochem. J.*, **64**, 481 (1956); DALGLIESH and DUTTON, *Biochem. J.*, **65**, 21P (1957).

Synthesis of carbohydrate from amino acids and other non-carbohydrate precursors (gluconeogenesis)

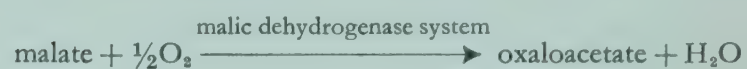
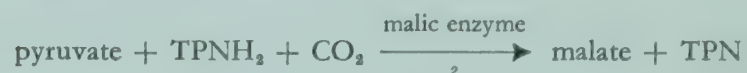
Glucose can be formed from lactate, pyruvate, glycerol and a number of amino acids: glutamic acid, aspartic acid, alanine, arginine, proline, hydroxyproline, histidine, serine, glycine and valine. The common metabolic property of all glucose-formers is the ability to yield pyruvate (or phosphopyruvate). The pathway from pyruvate to glucose includes most steps of the anaerobic glycolysis (Table 3, page 472) in reverse, but at three stages special reactions occur¹. These circumvent the energy barriers which would prevent a simple reversal of glycolysis. The three stages are:

Fig. 14 Pathways of carbohydrate breakdown and synthesis¹

The pathways differ at three points. Breakdown reactions are indicated by the left-hand arrows, synthesis reactions by the right-hand arrows



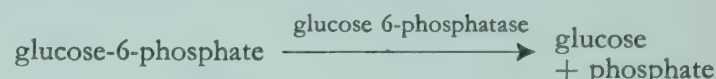
- (a) The formation of phosphopyruvate from pyruvate. The special reactions by which phosphopyruvate is formed are:



- (b) Fructose-1,6-diphosphate is converted into fructose-6-phosphate by a specific phosphatase⁴ (and not by transfer of phosphate to ADP):

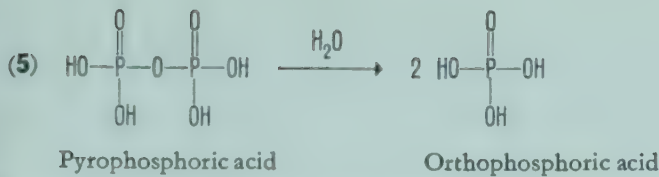


- (c) Glucose-6-phosphate is likewise dephosphorylated by a specific phosphatase⁵ (and not by transfer to ADP):

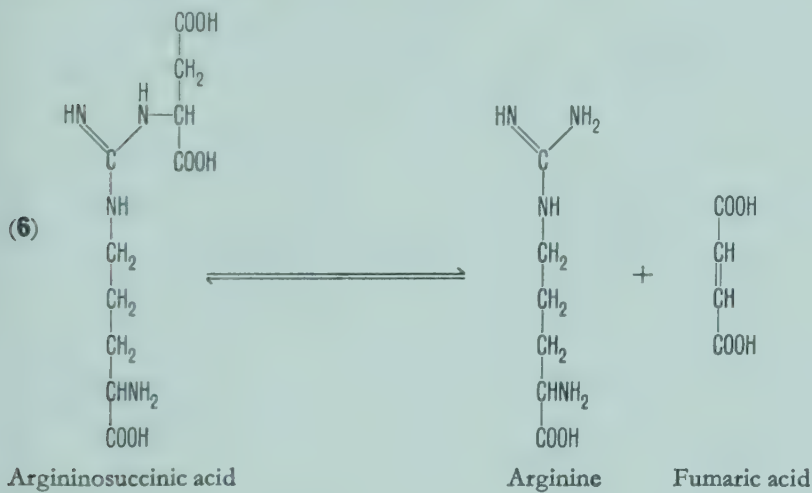


The stages of carbohydrate synthesis from pyruvate are summarized in Figure 14 opposite.

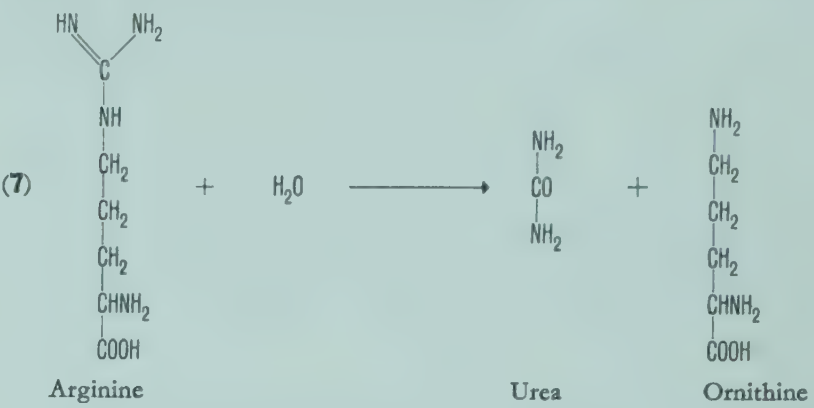
1) KREBS and KORNBERG, *Ergebn. Physiol.*, **49**, 212 (1957). 2) OCHOA et al., *J. biol. Chem.*, **174**, 979 (1948); VEIGA SALLES and OCHOA, *J. biol. Chem.*, **187**, 849 (1950); HARARY et al., *J. biol. Chem.*, **203**, 595 (1953). 3) UTTER and KURAHASHI, *J. biol. Chem.*, **207**, 821 (1954). 4) GOMORI, G., *J. biol. Chem.*, **148**, 139 (1943). 5) SWANSON, M. A., *J. biol. Chem.*, **184**, 647 (1950); CORI and CORI, *J. biol. Chem.*, **199**, 661 (1952).



Argininosuccinate reacts further to give arginine and fumarate¹⁰ by reaction (6):



This is followed by the hydrolysis of arginine to ornithine and urea. Ornithine can then undergo the same sequence of reactions, starting with reaction (3):



The cyclic sequence of the reactions is shown in Figure 15, below. As formulated here, one molecule each of carbon dioxide and ammonia are utilized for every molecule of urea produced. The second nitrogen atom of the urea molecule is supplied by aspartic acid. The latter is regenerated by transamination between glutamate and oxaloacetate. Glutamate in turn can be regenerated in two ways, either by transamination between various

Fig. 15 The urea cycle
A list of the enzymes involved in the cycle is given below the diagram

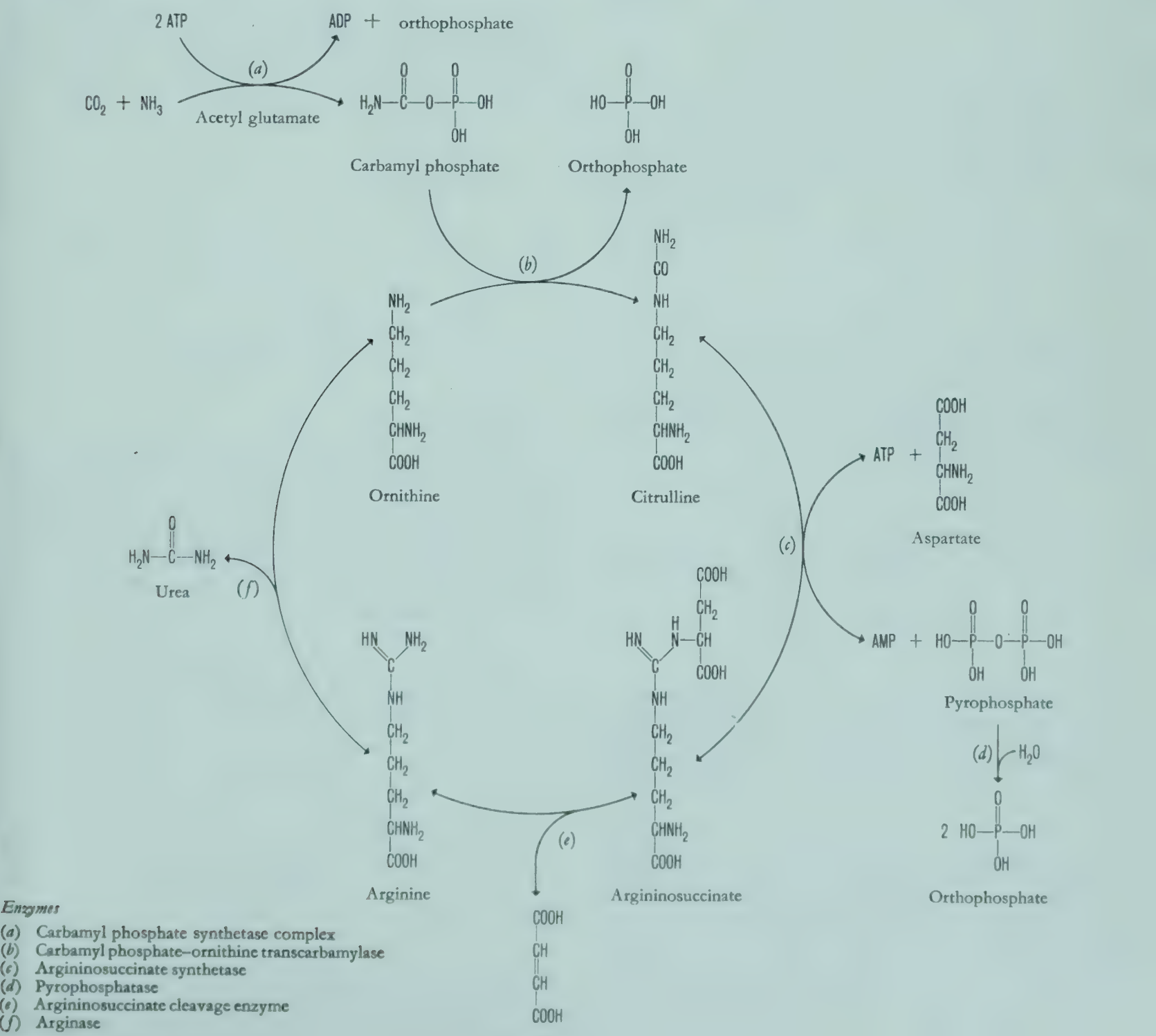
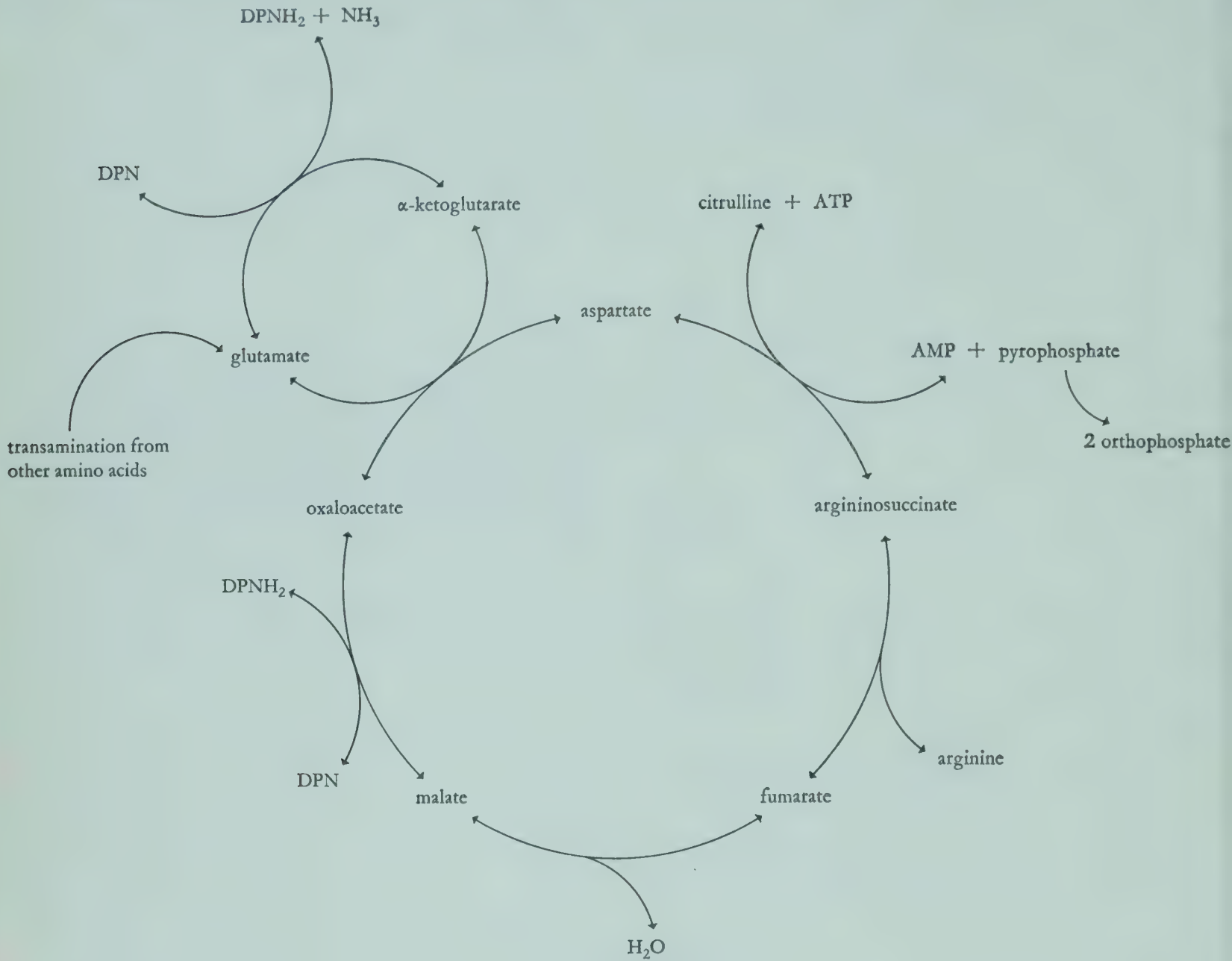
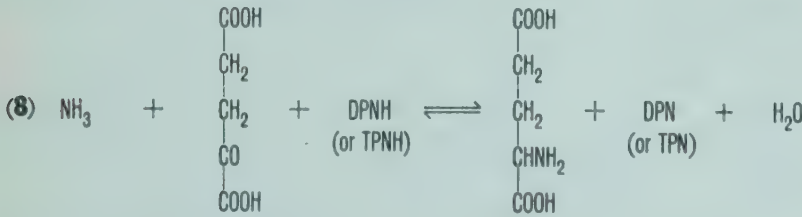


Fig. 16 Utilization and regeneration of aspartate in the synthesis of urea



amino acids and α-ketoglutarate (see page 476) or by reductive amination from ammonia and α-ketoglutarate¹¹:



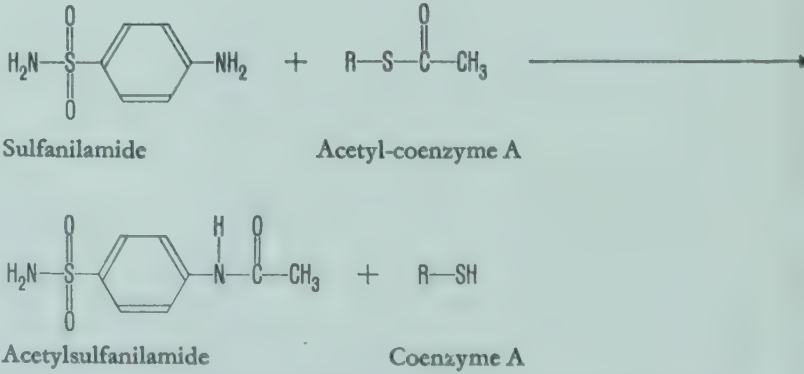
Ammonia α-Ketoglutaric acid Glutamic acid

The second nitrogen atom of urea must thus pass through glutamate and aspartate but not necessarily through the stage of ammonia. The supply of aspartate for reaction (4) involves two cycles which are subsidiary to the main urea cycle shown in Figure 15. These subsidiary processes are shown in Figure 16, above.

Acetylation of amines¹

Many aromatic and aliphatic amines are acetylated in the body. These include sulfanilamide, *p*-aminobenzoic acid, *p*-nitraniline and others². In general, the acetylated amines are less toxic than the unacetylated compounds. However, in some cases the low solubility of acetylated amines can render them harmful owing to their crystallization in the urinary tract.

The acetylation reaction proceeds via acetyl-coenzyme A (see page 474), for example:

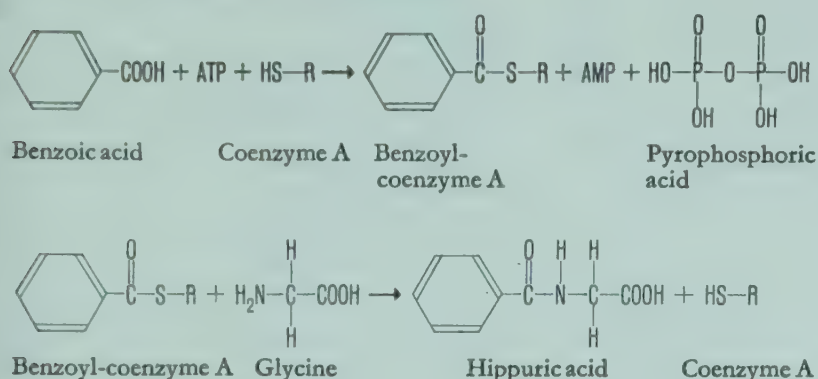


1) For reviews see KREBS, H. A., in SUMNER and MYRBÄCK (Eds.), *The Enzymes*, vol. II, part 2, New York, 1952, page 866; RATNER, S., *Advanc. Enzymol.*, **15**, 319 (1954). 2) KREBS and HENSELEIT, *Hoppe-Seyl. Z. physiol. Chem.*, **210**, 33 (1932). 3) JONES et al., *J. Amer. chem. Soc.*, **77**, 819 (1955). 4) METZENBERG et al., *J. biol. Chem.*, **229**, 1019 (1957). 5) GRISOLIA and COHEN, *J. biol. Chem.*, **204**, 753 (1953). 6) HALL et al., *Nature*, **178**, 1468 (1956). 7) BURNETT and COHEN, *J. biol. Chem.*, **229**, 337 (1957). 8) RATNER et al., *J. biol. Chem.*, **204**, 95 (1953). 9) RATNER and PETRACK, *Arch. Biochem. Biophys.*, **65**, 582 (1956). 10) RATNER et al., *J. biol. Chem.*, **204**, 115 (1953). 11) OLSON and ANFINSEN, *J. biol. Chem.*, **202**, 841 (1953).

1) TABOR et al., *J. biol. Chem.*, **204**, 127 (1953); LIPMANN, F., *Bact. Rev.*, **17**, 1 (1953). 2) WILLIAMS, R. T., *Detoxication Mechanisms*, London, 1947.

Formation of glycine conjugates

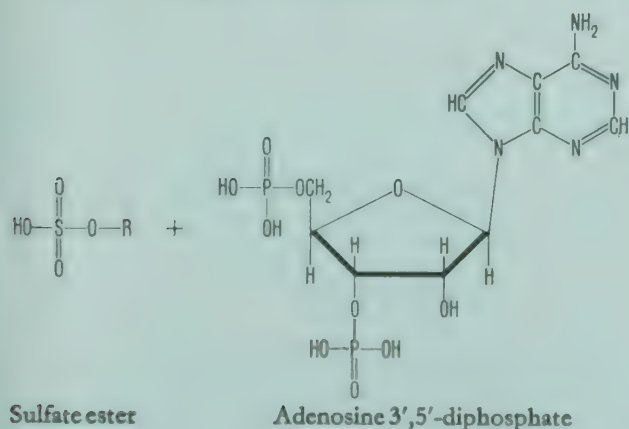
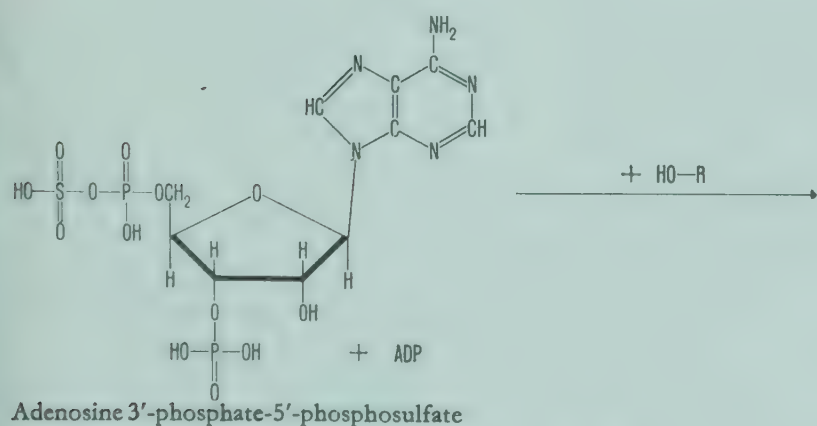
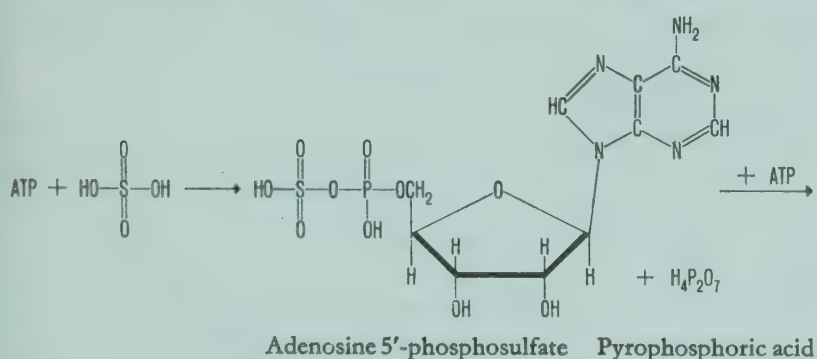
Aromatic acids such as benzoic acid, nicotinic acid, cinnamic acid and similar compounds are conjugated with glycine in various organs¹. The reaction requires coenzyme A and ATP, and proceeds by a mechanism similar to that involved in the activation of acetate (see page 474), for example:



1) CHANTRENNE, H., *J. biol. Chem.*, **189**, 227 (1951); SCHACHTER and TAGGART, *J. biol. Chem.*, **208**, 263 (1954); MOLDAVE and MEISTER, *J. biol. Chem.*, **229**, 463 (1957).

Formation of esters of sulfuric acid

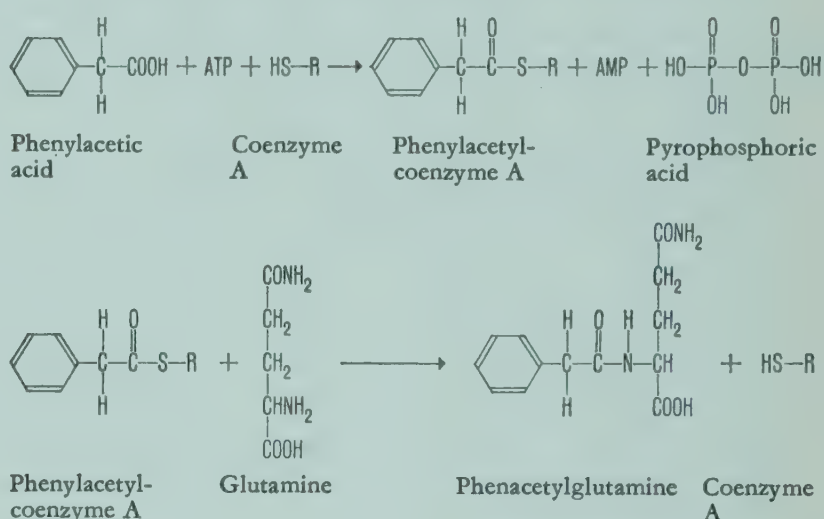
Naturally occurring sulfate esters include the polysaccharides chondroitin sulfate and heparin, steroid sulfates and phenyl sulfates (aryl sulfates). In addition to these substances, foreign phenols when ingested are esterified with sulfate to a greater or lesser extent, and the elimination of phenols in the form of phenyl sulfates constitutes one of several detoxication mechanisms of phenols¹. Sulfate ester formation requires inorganic sulfate and ATP and involves the formation of two "active sulfate" intermediates²:



1) WILLIAMS, R. T., *Detoxication Mechanisms*, London, 1947. 2) BANDURSKI et al., *J. Amer. chem. Soc.*, **78**, 6408 (1956); ROBBINS and LIPMANN, *ibid.*, **78**, 2652, 6409 (1956); ROBBINS and LIPMANN, *J. biol. Chem.*, **229**, 837 (1957); GREGORY and LIPMANN, *ibid.*, **229**, 1081 (1957).

Formation of phenacetylglutamine

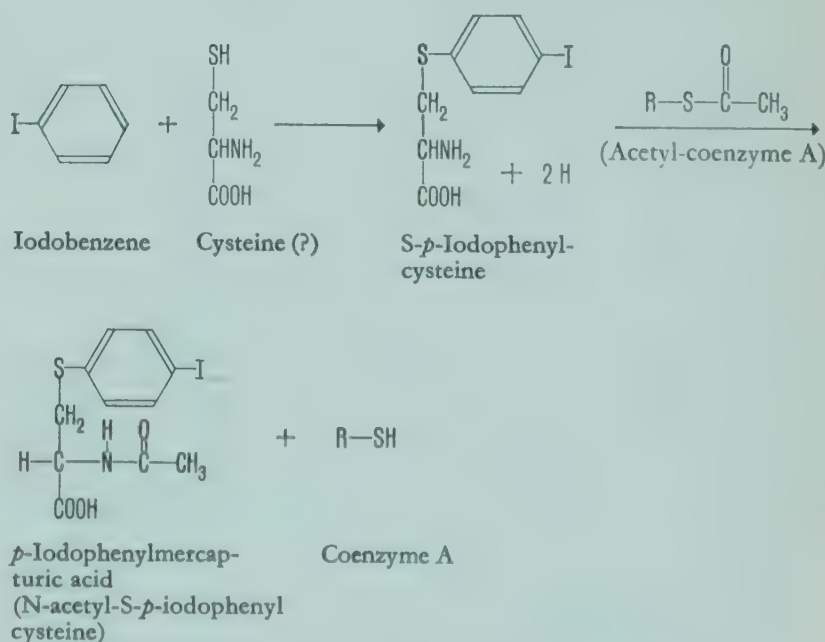
This detoxication mechanism is peculiar to the detoxication of phenylacetic acid in anthropoid apes and man. The reaction requires coenzyme A and ATP, and proceeds by a mechanism similar to that involved in the activation of acetate (see page 474):



The first of these reactions occurs in beef as well as human tissues; the second however, appears to be confined to human kidney and liver, and it has been found not to occur in rat and beef liver. As in the case of acetate activation, phenylacetic acid and ATP can be replaced by phenylacetyl-AMP, but an accumulation of the latter on incubating phenylacetic acid on ATP has not been demonstrated.

Formation of mercapturic acids

A number of aromatic compounds (e.g. halogenobenzenes, naphthalene) give rise on ingestion to mercapturic acids (N-acetyl-S-aryl cysteines)¹. The mechanism of formation of these compounds is not known, but it probably proceeds as follows^{1,2}:



1) WILLIAMS, R. T., *Detoxication Mechanisms*, London, 1947. 2) MILLS and WOOD, *J. biol. Chem.*, **207**, 695 (1954).

A	page	A	page	A	page
Acetals	427	Adenosine diphosphoflavin ribitol	461	Aminoacetic acid. See Glycine	
Acetaldehyde, formation from β -alanine	482	- diphosphonotinamide riboside. See DPN		Amino acids	445 sq
- in alcoholic fermentation	473	- enzymic deamination	498	- carbohydrate synthesis from	514, 515
- in 2-desoxyribose-5-phosphate degradation	482	- 5'-monophosphate. See AMP		- deamination and transamination	476, 477
- in L-threonine degradation	480	- 3'-phosphate 5'-phosphosulfate	463	- decarboxylation	477
Acetaldehyde-TPP complex in pyruvate oxidation	474	- in formation of sulfate esters	519	- degradation	476 sq
Acetate, biosynthesis of cholesterol from	503	- 5'-phosphosulfate	463	- formation of basic cell constituents from	508 sq
Acetoacetic acid (acetoacetate), formation from acetyl-coenzyme A	476	- in formation of sulfate esters	519	- glucogenic, cell constituents and metabolites from	508
- in fatty-acid degradation	476	- triphosphate. See ATP		- hydroxy-, degradation	479, 480
- in leucine degradation	478	Adenosine deaminase	484, 498	- microbiological assay	446 sq
- in lysine degradation	481	- in adenylic acid degradation	483	- natural, configuration	445
- in phenylalanine and tyrosine degradation	481	S-Adenosylmethionine	511, 512	- nonessential, formation of	507
Acetoacetyl-coenzyme A, formation from acetyl-coenzyme A	476	Adenylate kinase in biological energy transformations	486	- formation from glucose	499
- in biosynthesis of cholesterol	503	Adenylic acid. See AMP		- occurring in free form	450, 451
- in fatty-acid degradation	476	Adenylic deaminase	483, 484, 498	- in proteins	446 sq
Acetoacetyl-deacylase in fatty-acid degradation	476	Adenylosuccinic acid in formation of adenylic acid	510	- quantitative estimation	445
Acetone, formation from acetyl-coenzyme A	476	Adipose tissue, fermentation and respiration rates in	470, 471	D-Amino acid oxidase	476
- dihydroxy-. See Dihydroxyacetone		Adonitol	439	- in D-ornithine degradation	478
Acetone bodies (ketone bodies)	475, 476	D-Adonose. See D-Ribulose		L-Amino acid oxidase	476
Acetonedicarboxylic acid in lysine degradation	481	ADP (adenosine diphosphate)	459	α -Aminoacrylic acid, in L-cysteine and cystine degradation	480
N-Acetyl-S-arylcysteines, formation	519	- in carbohydrate synthesis	515	- in serine degradation	479
Acetylation as detoxication mechanism	516	- in CO ₂ -fixation by phosphopyruvate	502	Aminoacyl adenosine monophosphates	462
Acetylcholine, enzymic hydrolysis	495	- in glutathione formation	512	α -Amino adipic acid	450
Acetylcholine, formation and function	508	- in glycolysis	472, 473	- in lysine degradation	481
Acetylcholine esterase	495	- in formation of guanylic acid	511	α -Amino adipic semialdehyde in lysine degradation	481
Acetyl-coenzyme A, acetylation of choline by	508	- in formation of inosinic acid	509	2-Aminobenzoylpyruvic acid in tryptophan degradation	482
- biosynthesis of cholesterol from	503	- in isoleucine degradation	479	α -Amino-n-butyric acid	450
- from fatty acids	474, 476	- in biosynthesis of pyrimidines	513	- degradation	479
- from cholesterol degradation	482	- in biosynthesis of urea	516 sq.	γ -Amino-n-butyric acid	450
- from degradation of foods	484, 485	- phosphorylation	486	- formation from glutamic acid	477
- in acetylation of amines	518	ADP aspartic acid	462	- function	508
- in leucine degradation	478	ADP glutamic acid	462	- transamination	477
- in isoleucine degradation	479	Adrenals, esterases in	495	β -Amino isobutyric acid	450
- in norleucine degradation	479	- fermentation and respiration rates in	470, 471	- excretion	482
- in formation of mercapturic acids	519	- phospholipase in	496	- in thymine degradation	484
- in norvaline degradation	479	Adrenal cortex, pituitary control	505	α -Amino-n-caproic acid. See Norleucine	
- in phenylalanine and tyrosine degradation	481	Adrenal steroids, catabolism and excretion	505	α -Amino isocaproic acid. See Leucine	
- in pyruvate oxidation	474	- synthesis and metabolism	503 sq.	α -Amino- γ -carbamylobutyric acid. See Glutamine	
- in serine degradation	479	Adrenaline, function	508	α -Amino- β -carbamylopropionic acid (asparagine)	446
- in L-threonine degradation	480	- formation from tyrosine	513	5-Amino-4-carboxamidoimidazole ribotide in formation of inosinic acid	510
- in tricarboxylic acid cycle	473, 474	Adrenocorticotrophic hormone	505	5-Amino-4-carboxyimidazole ribotide in formation of inosinic acid	510
N-Acetyl-L-cysteine derivatives in urine	446	Adrenosterone, synthesis from cholesterol	504, 505	α -Aminocrotonic acid in homoserine degradation	480
N-Acetyl-D-galactosamine	434	<i>Aerobacter aerogenes</i> , L-histidine degradation in	478	2-Aminoethanesulfonic acid. See Taurine	
- enzymic hydrolysis	494	α -Alanine	446	α -Aminoglutaric acid. See Glutamic acid	
N-Acetyl-D-glucosamine	434	- degradation	477	α -Amino- δ -guanido-n-valeric acid. See Arginine	
N-Acetylglucosaminides, enzymic hydrolysis	494	- formation from glucose	499	2-Amino-3-hydroxybenzoylpyruvic acid in tryptophan degradation	482
Acetyl glutamate in biosynthesis of urea	516, 517	- in tryptophan degradation	482	α -Amino- β -hydroxybutyric acid. See Threonine	
N-Acetyl-S-p-iodophenylcysteine	519	- residues, enzymic hydrolysis	490	α -Amino- γ -hydroxybutyric acid. See Homoserine	
S-Acetyl- α -lipoic acid in pyruvate oxidation	474	- transamination	477	α -Amino- β -(p-hydroxyphenyl)propionic acid. See Tyrosine	
Acetyl- β -methylcholine, enzymic hydrolysis	495	β -Alanine	450	α -Amino- β -hydroxypropionic acid. See Serine	
Acetylsulfanilamide as detoxication product	516	- formation and function	508	5-Aminoimidazole-4-carboxamide ribotide	458
Acids, aliphatic, branched-chain, detoxication in body	516	- formation from aspartic acid	477	α -Amino- β -(4-imidazole)propionic acid. See Histidine	
- aromatic, conjugation with glycine	519	- in cytosine and uracil degradation	484	5-Aminoimidazole ribotide	458
- - detoxication in body	516	- transamination with α -ketoglutarate	477, 482	- in formation of inosinic acid	509, 510
- α -ketonic. See α -Ketonic acids		D-Alanyl-L-histidine, enzymic hydrolysis	492	α -Amino- β -(3-indolyl)propionic acid. See Tryptophan	
Aconitase, action on <i>cis</i> -aconitic acid	481	L-Alanyl-L-histidine, enzymic hydrolysis	492	α -Amino- β -keto adipic acid, in glycine degradation	480
- in tricarboxylic acid cycle	473	β -Alanyl-L-histidine, enzymic hydrolysis	492	- in biosynthesis of porphyrins	511
<i>cis</i> -Aconitic acid (<i>cis</i> -aconitate), action of aconitase on	481	Alcaptonuria	481	δ -Aminolevulinic acid	450
- in tricarboxylic acid cycle	473, 474	Alcoholic fermentation	470, 473	- in glycine degradation	480
ACTH, control of adrenal cortex by	505	Alcohols, detoxication in body	516	- in biosynthesis of porphyrins	511
Acyl-adenosine monophosphates	462	- polyhydric	431, 439	α -Amino- γ -methylthiolbutyric acid. See Methionine	
Acyl-adenylate in fatty-acid oxidation	474	Aldehydes, enzymic oxidation	498	α -Amino- β -methyl-n-valeric acid. See <i>iso</i> Leucine	
Acyl-coenzyme A from fatty-acid oxidation	474, 475	Aldolase, in 2-desoxyribose-5-phosphate degradation	482	α -Amino- β -phenylpropionic acid. See Phenylalanine	
Acyl-dehydrogenase in fatty-acid oxidation	475	- in glycolysis	472, 473	α -Aminopropionic acid. See α -Alanine	
Acylglucuronides, formation, as detoxication mechanism	516	- «hydroxyamino acid»	480	β -Aminopropionic acid. See β -Alanine	
Acyl phosphatase	495	Aldonic acids	431, 440	Aminosuccinic acid. See Aspartic acid	
Acyl phosphates, enzymic hydrolysis	495	Aldoses	427, 428	5-Amino-4-succinocarboxamidoimidazole ribotide in formation of inosinic acid	510
ADDISON'S disease, aldosterone in	505	Aldosterone	505	α -Amino- β -thiolpropionic acid. See Cysteine	
Adenase	484	- synthesis from cholesterol	504, 505		
- in adenylic acid degradation	483, 484	Aldosteronism, primary	505		
Adenine	454	D-Aldo-sugars, configurational relationships	429		
- degradation	483, 484	Alkaline phosphatase	495		
- desoxyriboside. See Desoxyadenosine		Alkaptonuria	481		
- in adenylic acid degradation	483	Alkyl halides, detoxication in body	516		
- nucleotide. See AMP		Alkylglucuronides, formation, as detoxication mechanism	516		
- riboside. See Adenosine		Allantoin, degradation	484		
- ribotide. See AMP		- in purine metabolism	483, 484		
Adenosine	455	D-Allose, structure	429		
- in adenylic acid degradation	483	<i>iso</i> Alloxazine	452		
- diphosphate (pyrophosphate). See ADP		D-Allulose, structure	430		
- 3',5'-diphosphate, in formation of sulfate esters	519	Altroheptulose, structure	430		
		D-Altrose, structure	429		
		Amines, acetylation in body	518		
		Amine oxidase in degradation of 5-hydroxy-tryptamine	514		
		«Amine ribotide» in formation of inosinic acid	509		

A	page
Aminotripeptidase	491, 492
α -Amino- δ -urcido- <i>n</i> -valeric acid. See Citrulline	
α -Aminoisovaleric acid. See Valine	
α -Amino- α -vinylacetic acid, in L-homocysteine degradation	480
- in homoserine degradation	479
Ammonia, synthesis of urea from carbon di- oxide and	516, 517
AMP (adenosine 5'-monophosphate, 5'-ade- nylic acid)	459
- degradation	483, 484
- enzymic deamination	498
- enzymic hydrolysis	498
- formation	510, 511
- in conjugation of bile acids	512
- in fatty-acid degradation	476
- in formation of inosinic acid	509, 510
- in biosynthesis of urea	516 sq.
- phosphorylation	486
Amygdalin, enzymic hydrolysis	493
α -Amylase	493
α -Amylase dextrins, enzymic hydrolysis	493
Amylo-1,6-glucosidase	493
Amylopectin	442
- enzymic hydrolysis	493
Amylose (β -amylose)	442
- enzymic hydrolysis	493
α -Amylose	442
β -Amylose. See Amylose	
Amylum. See Starch	
Androgens, synthesis by testis	505
Δ^4 -Androstene-3,17-dione, synthesis from cholesterol	504 sq.
- metabolism	506, 507
Anthranilic acid in tryptophan degradation	481, 482
Apo-enzymes	467
D-Arabinose	429, 432
DL-Arabinose	432
D-Arabulose. See D-Ribulose	
Arbutin, enzymic hydrolysis	493
Argentaffinoma, 5-hydroxyindoleacetic acid in	514
Arginase in biosynthesis of urea	517
L-Arginine	446
- cell constituents and metabolites from	508
- creatine formation from glycine, methio- nine and	511
- degradation	478
- in L-citrulline degradation	478
- in biosynthesis of urea	517, 518
- residues, enzymic hydrolysis	489
- transamination	477
Argininosuccinate in biosynthesis of urea 516 sq.	
Argininosuccinate cleavage enzyme in bio- synthesis of urea	517
Argininosuccinate synthetase in biosynthesis of urea	517
Arylglyceronides, formation, as detoxication mechanism	516
L-Ascorbic acid	440
Asparagine	446
L-Aspartic acid (L-aspartate)	446
- β -alanine formation from	508
- cell constituents and metabolites from	508
- decarboxylation	477
- degradation	477
- formation from glucose	499
- in formation of adenylic acid	510
- in formation of inosinic acid	510
- in biosynthesis of pyrimidines	513
- in biosynthesis of urea	516 sq.
- β -monoamide	446
- regeneration in urea synthesis	518
- transamination	476
ATP (adenosine triphosphate)	459
- in conjugation of bile acids	512
- in biological energy transformations	486
- in biosynthesis of cephalin and lecithin	502
- in fatty-acid oxidation	474 sq.
- in glutamine formation	508
- in glutathione formation	512
- in formation of glycine conjugates	519
- in glycolysis	472, 473
- in formation of guanylic acid	511
- in formation of inosinic acid	509, 510
- in leucine degradation	478
- in isoleucine degradation	479
- in detoxication of phenylacetic acid	519
- in CO ₂ -fixation by phosphopyruvate	502

A	page
ATP in breakdown and synthesis of glycogen 515	
- in biosynthesis of pyrimidines	513
- in biosynthesis of urea	516 sq.
- reaction with creatine	512
Azotobacter, respiration rate	471
B	
Bacteria, esterases of	495
- threonine degradation by	480
Bee venom, phospholipase of	496
Benzoic acid, conjugation with glycine	514
- detoxication in body	516
- excretion	447
Benzoylglucuronide as detoxication product 516	
Bile acids, conjugation and excretion	512
- function	508
Bile acyl-coenzyme A in conjugation of bile acids	512
Biological energy transformations, role of ATP in	486
Biological oxidations, mechanism	485
Blood, esterases	495
- glycosidases	493, 494
Blood cells, white, esterases	495
- fermentation rates in	470, 471
Blood-group A and O(H) substances, enzymic hydrolysis	494
Blood plasma, esterases	495
Blood serum, proteases	492
Blood sugar. See D-Glucose	
Bone, esterases	495
Bone marrow, red, fermentation and respira- tion rates in	470, 471
Brain, amino acids	450
- cortex, fermentation and respiration rates in	470, 471
- esterases	495
- glycosidases	494
- transamination reactions in	477
- white matter, respiration rates in	470
Brain sugar. See D-Galactose	
Butyrylcholine, enzymic hydrolysis	495
isoButyryl-coenzyme A in valine degradation 479	
C	
Cadaverine, formation from lysine	477
Cane sugar	441
isoCaproic acid, from cholesterol degradation 482	
- in synthesis of adrenocortical steroids	504
Carbamate in biosynthesis of urea	516
Carbamyl- β -alanine in cytosine and uracil degradation	484
Carbamyl- β -aminoisobutyric acid in thymine degradation	484
Carbamylaspartic acid	450
- in biosynthesis of pyrimidines	513
Carbamyl phosphate, in biosynthesis of pyri- midines	513
- in biosynthesis of urea	516, 517
Carbamyl phosphate-aspartate transcarbamyl- ase in biosynthesis of pyrimidines	513
Carbamyl phosphate-ornithine transcarbamyl- ase in biosynthesis of urea	517
Carbamyl phosphate synthetase complex in urea synthesis	517
Carbohydrates (sugars)	427 sq.
- breakdown and synthesis	515
- degradation	472 sq.
- oxidation	473, 474
- primary oxidation products	431, 440
- stereochemistry	427 sq.
- synthesis from noncarbohydrate precu- sors	514, 515
Carbon chains, extension by CO ₂ -fixation 502, 515	
Carbon dioxide, synthesis of urea from am- monia and	516, 517
- fixation, extension of carbon chains by	502
Carboxypeptidase	490, 492
Carcinoid, malignant, 5-hydroxyindoleacetic acid in	514
Cardiac infarction, plasma transaminase in	477
Carnosinase	492
Cartilage, costal, fermentation and respiration rates in	470, 471
α -Casein, separation from peptones	488
Catalysis of biological oxidations	485
Cathepsins	491, 492
Cathepsin IV (Carboxypeptidase)	492
CDP. See Cytidine diphosphate	

C	page
Cells, constituents, biosynthesis	499 sq.
- metabolism	471
- metabolites, formation from amino acids	508 sq.
- formation from glucose	499 sq.
Cellobiose	441
- enzymic hydrolysis	493
Cellulose	442
Cephalin, biosynthesis	502
- enzymic hydrolysis	496
Cerebrose. See D-Galactose	
Chitin	442
Chitosamine. See D-Glucosamine	
Δ^7 -Cholesten-3 β -ol in biosynthesis of choles- terol	503
Cholesterol, biosynthesis	503
- degradation	482
- estrogen synthesis from	506, 507
- skeleton, numbering:	504
- synthesis of adrenocortical hormones from	504, 505
Choline, acetylation by acetyl-coenzyme A	508
Choline esterases	495
- formation and function	508
- in biosynthesis of lecithin	502
Choline phosphokinase, in biosynthesis of lecithin	502
Chondroitin sulfate	443
- formation	519
- enzymic hydrolysis	494
D-Chondrosamine	433
Chymotrypsins	489, 490
Chymotrypsinogen B	489
α -Chymotrypsinogen	489
Cis-trans-isomerase in phenylalanine and ty- rosine degradation	481
Citric acid (citrate), formation, from <i>cis</i> - aconitic acid	481
- from glucose	499
- in tricarboxylic acid cycle	473, 474
isoCitric acid (isocitrate), formation from <i>cis</i> -aconitic acid	481
- in tricarboxylic acid cycle	473, 474
Citric acid cycle. See Tricarboxylic acid cycle	
isoCitric dehydrogenase in tricarboxylic acid cycle	473
L-Citrulline	450
- degradation	478
- in biosynthesis of urea	516, 517
Clostridium species, phospholipase of	497
CMP. See Cytidine monophosphate	
CoA. See Coenzyme A	
Codehydrogenases	452
Codehydrogenase II. See TPN	
Coenzymes	467
- and activators	469
- nucleotide	452 sq., 460 sq.
Coenzyme A	461
- acetyl-. See Acetyl-coenzyme A	
- in conjugation of bile acids	512
- in biosynthesis of cephalin	502
- in formation of neutral fat	503
- in fatty acid oxidation	474, 476
- in formation of glycine conjugates	519
- in glycine degradation	480
- in homoserine degradation	480
- in biosynthesis of lecithin	502
- in L-leucine degradation	479
- in isoleucine degradation	479
- in formation of mercapturic acids	519
- in norleucine degradation	479
- in detoxication of phenylacetic acid	519
- in phenylalanine degradation	481
- in pyruvate oxidation	474
- in serine degradation	479
- in L-threonine degradation	480
- in tricarboxylic acid cycle	473, 474
- in tyrosine degradation	481
- in valine degradation	479
Coenzyme II. See TPN	
Colonic mucosa, respiration rates in	470
Connective tissue, respiration rates in	470
«CORT Ester». See α -D-Glucose-1-phosphate	
Corn sugar. See D-Glucose	
Cornea, glycosidases	494
Corticoids, Corticosteroids. See Adrenal steroids	
Corticosterone	505
- synthesis from cholesterol	504, 505
Corticotropin (ACTH)	505
Cortisol, synthesis from cholesterol	504, 505

C	page
Cortisone, synthesis from cholesterol . . .	504, 505
Creatine	450
- formation	511
- function	508
- phosphate, formation in tissues . . .	511, 512
- reaction with ATP	512
Creatinine	451
Crotonase in leucine degradation	478
CTP. See Cytidine triphosphate	
L-Cystathionine	451
- in L-homocysteine degradation . . .	480
L-Cysteic acid	451
- decarboxylation	477
L-Cysteine	446
- cell constituents and metabolites from .	508
- degradation	480
- formation from glucose	499
- in glutathione formation	512
- in L-homocysteine degradation . . .	480
- in formation of mercapturic acids . .	519
- taurine formation from	512
Cysteinesulfinic acid in biosynthesis of tau-	
rine	512
Cystine	446
- degradation	480
Cytidine	455
- monophosphate (CMP)	459
- in biosynthesis of lecithin and cephalin .	502
- diphosphate (CDP)	459
- diphosphate choline	466
- in biosynthesis of lecithin	502
- diphosphate ethanolamine	466
- diphosphate glycerol	465
- diphosphate ribitol	466
- triphosphate (CTP)	459
- in biosynthesis of cephalin and lecithin .	502
- in biosynthesis of pyrimidines . . .	513
Cytidylic acid, enzymic hydrolysis	498
Cytochromes, electron transport in, in cells .	485
Cytosine	454
- degradation	482, 484
- desoxyriboside. See Desoxycytidine	
- riboside. See Cytidine	

D	page
DADP (desoxyadenosine diphosphate) . . .	459
DAMP (desoxyadenosine monophosphate) .	459
DATP (desoxyadenosine triphosphate) . .	459
DCDP (desoxycytidine diphosphate) . . .	459
DCMP (desoxycytidine monophosphate) . .	459
DCTP (desoxycytidine triphosphate) . . .	459
Deacylase, acetoacetyl-, in fatty-acid degrada-	
tion	476
Deaminases	498
- purine	484
Deaminase, adenosine	484, 498
- adenylic	483, 484, 498
- guanosine	484, 498
- guanylic	498
Deamination, oxidative	476, 477
Decarboxylases	477
Decarboxylase, oxalosuccinic, in tricarboxylic	
acid cycle	473
Decarboxylation of amino acids	477
Dehydrase, serine, in serine degradation .	479
11-Dehydrocorticosterone, synthesis from	
cholesterol	504, 505
Dehydrogenase, acyl-, in fatty-acid oxidation	
- isocitric, in tricarboxylic acid cycle . .	473
- dihydroorotic, in biosynthesis of pyrimi-	
dines	513
- glucose-6-phosphate, in pentose-phosphate	
cycle	501
- L-glutamic	476
- glycerophosphate, in formation of glycerophos-	
phates from glucose	499
- β -hydroxyacyl-, in fatty-acid oxidation . .	475
- β -hydroxybutyric, in fatty-acid degradation	
476	
- α -ketoglutaric, in tricarboxylic acid cycle .	473
- lactic, in glycolysis	472
- malic, in carbohydrate synthesis	515
- in tricarboxylic acid cycle	473
- succinic, in tricarboxylic acid cycle . .	473
- triose-phosphate, in glycolysis	472
Deoxy-. See Desoxy-	
Desoxyadenosine	455
- enzymic deamination	498
- monophosphate	459
Desoxyadenosine diphosphate	459
- triphosphate	459

D	page
2-Desoxy-D-altromethyllose	432
Desoxyarabinose. See 2-Desoxy-D-ribose	
Desoxycorticosterone	505
- synthesis from cholesterol	504, 505
Desoxycytidine	456
- monophosphate	459
- diphosphate	459
- triphosphate	459
2-Desoxy-D-erythropentose. See 2-Desoxy-D-	
ribose	
6-Desoxy-L-galactose	432
Desoxyguanosine	455
- monophosphate	459
- diphosphate	459
- triphosphate	459
(Desoxy)-5-hydroxymethylcytidine mono-	
phosphate	459
Desoxyinosine	457
6-Desoxy-L-mannose	432
(Desoxy)-5-methylcytidine monophosphate .	459
Desoxyribonucleases	487, 488, 497
Desoxyribonucleic acids (DNA)	452, 453
- enzymic cleavage	487, 488, 497
Desoxyribonucleotides	453
- enzymic degradation	498
2-Desoxy-D-ribose	432
2-Desoxyribose-1-phosphate	436
2-Desoxyribose-5-phosphate	436
- degradation of	482
- formation from glucose	499
(Desoxy)thymidine	456
- monophosphate	459
- diphosphate	459
- triphosphate	459
Desoxyxanthosine	457
Detoxication mechanisms	516 sq.
Dextran	443
Dextrins, enzymic hydrolysis	493
Dextronic acid. See D-Gluconic acid	
DGDP (desoxyguanosine diphosphate) . . .	459
DGMP (desoxyguanosine monophosphate) .	459
DGTP (desoxyguanosine triphosphate) . .	459
(D)HMCMP ([desoxy]-5-hydroxymethylcyti-	
dine monophosphate)	459
α,ϵ -Diamino- <i>n</i> -caproic acid. See Lysine	
α,ϵ -Diamino- δ -hydroxy- <i>n</i> -caproic acid	
(δ -hydroxylysine)	447
α,ϵ -Diaminopimelic acid, decarboxylation .	477
Di-(α -aminopropionic)- β -disulfide. See Cys-	
tine	
2,5-Diamino- <i>n</i> -valeric acid. See Ornithine	
N,N'-Dibenzoylornithine, excretion	451
Diesterase, glycerylphosphorylcholine . .	497
Digestion	472
Digestive enzymes	487 sq.
D-Digitoxose	432
D- α - β -Diglycerides, formation of neutral fat	
from	503
- in biosynthesis of lecithin and cephalin . .	502
Dihydroorotic acid in biosynthesis of pyri-	
midines	513
Dihydroorotic dehydrogenase in biosynthesis	
of pyrimidines	513
Dihydrothymine in thymine degradation . .	484
Dihydrouracil in cytosine and uracil degrada-	
tion	482
Dihydroxyacetone	432
- phosphate	435
- in formation of glycerophosphates from	
glucose	499
- in breakdown and synthesis of glycogen .	515
- in glycolysis	472, 473
- in pentose-phosphate cycle	501
- relation to keto-sugars	430
5,6-Dihydroxyindole in melanin formation .	514
3,4-Dihydroxyphenylethylamine, decarboxylation	
- in biosynthesis of adrenaline and noradre-	
naline	513
- in melanin formation	514
3,4-Dihydroxyphenylethylamine, formation	
from 3,4-dihydroxyphenylalanine	477
- in biosynthesis of adrenaline and noradre-	
naline	513
2,5-Dihydroxyphenylpyruvic acid in phenyl-	
alanine and tyrosine degradation	481
3,5-Diiodotyrosine	446
Diketohydrindylidenediketohydrindamine .	445
Dipeptidases	491, 492
Dipeptidase, glycylglycine	491, 492
Dipeptidase, glycyl-L-leucine	491, 492
Dipeptides, enzymic hydrolysis	491

D	page
Diphosphatase, hexose, dephosphorylation of	
fructose-1,6-diphosphate by	515
1,3-Diphosphoglyceric acid. See Glyceric acid	
1,3-diphosphate	
Diphosphopyridine nucleotide. See DPN	
Disaccharides	441
(D)MCMP ([desoxy]-5-methylcytidine mono-	
phosphate)	459
DNA. See Desoxyribonucleic acids	
«Dopa». See 3,4-Dihydroxyphenylalanine	
DPN (diphosphopyridine nucleotide) . . .	460
- enzymic hydrolysis	496
- in alcoholic fermentation	473
- in aspartate regeneration in urea synthesis	
518	
- in amino-acid and fatty-acid degradation .	476
- in glutamate regeneration in urea synthesis	
518	
- in glycolysis	472, 473
- in homoserine degradation	480
- in lactate-pyruvate conversion	473
- in leucine degradation	478
- in isoleucine degradation	479
- in norleucine degradation	479
- in biosynthesis of pyrimidines	513
- in pyruvate oxidation	474
- in serine degradation	479
- in L-threonine degradation	480
- in tricarboxylic acid cycle	473
- in valine degradation	479
- in formation of xanthidylic acid	511
- reduced, in alcoholic fermentation . . .	473
- in amino-acid degradation	476
- in fatty-acid degradation	476
- in aspartate regeneration in urea syn-	
thesis	518
- in glutamate regeneration in urea syn-	
thesis	518
- in biosynthesis of glutamic acid	507
- in glycolysis	472, 473
- in homoserine degradation	480
- in biosynthesis of hydroxyproline	507
- in lactate-pyruvate conversion	473
- in leucine degradation	478
- in isoleucine degradation	479
- in norleucine degradation	479
- in biosynthesis of proline	507
- in biosynthesis of pyrimidines	513
- in pyruvate oxidation	474
- in serine degradation	479
- in L-threonine degradation	480
- in valine degradation	479
- in formation of xanthidylic acid	511
DPNH, DPNH ₂ . See DPN, reduced	
(D)TDP ([desoxy]thymidine diphosphate) .	459
(D)TMP ([desoxy]thymidine monophos-	
phate)	459
(D)TTP ([desoxy]thymidine triphosphate) .	459
isoDulcitol	432

E	page
Echinoderm venom, phospholipase of	496
Electron transfer in biological oxidations .	485
Embryo, fermentation rates in	471
Enantiomorphs	427, 428
Endocrine tissues, glycosidases of	494
Endopeptidases	487
Energy metabolism	470 sq.
Energy-supplying reactions	472 sq.
Enolase in glycolysis	472
Enoylhydase in fatty-acid oxidation	475
Enterokinase	489
Enzymes	467 sq.
- mechanism of action	467
- catalyzing biological oxidations	485
- digestive	487 sq.
- inhibition	468, 469
- proteolytic. See Proteases	
- specificity	467
Enzyme kinetics	467 sq.
Epinephrine. See Adrenaline	
Ergothioneine	451
Erythrocytes, esterases	495
- fermentation and respiration rates in .	470, 471
- proteases	492
D-Erythrose	429, 432
D-Erythrose-4-phosphate	435
- in pentose-phosphate cycle	500, 501
D-Erythrulose, structure	430
L-Erythrulose	432
L-Erythrulose-1-phosphate	435
Esterases	487, 495, 496

E	page
Esterases of tissues	495
Esterase, acetylcholine	495
Estradiol, biosynthesis and metabolism	506, 507
Estriol, biosynthesis and metabolism	506, 507
Estrogens, biosynthesis and metabolism	506, 507
- synthesis by ovary	505
Estrone, biosynthesis and metabolism	506, 507
Ethanolamine, formation and function	508
- formation from serine	477
- in biosynthesis of cephalin	502
- in choline formation from serine	508
β -Ethylacrylyl-coenzyme A in norleucine degradation	479
Exopeptidases	487, 490, 491
- precursors	490, 491

F	page
FAD. See Flavin adenine dinucleotide	
Farnesic acid in biosynthesis of cholesterol	503
Fats, enzymic hydrolysis	495
- formation	499, 503
- oxidative degradation	474 sq.
«Fatty acid cycle»	474
Fatty acids, formation from glucose	499
- in biosynthesis of lecithin and cephalin	502
- oxidation	474 sq.
- β -oxidation	475
- unsaturated, degradation of	475
Fermentation, alcoholic	470, 473
- lactic acid	470 sq.
«FISCHER-BAER Ester». See D-Glyceraldehyde 3-phosphate	
FISCHER projection formulas	428
Flavin adenine dinucleotide (FAD)	461
- enzymic hydrolysis	496
Flavin mononucleotide. See FMN	
Flavin nucleotides as enzyme prosthetic groups	485
Flavin ribityl phosphate. See FMN	
Flavoproteins in oxidative deamination	476
FLEXNER'S carcinoma, fermentation and respiration rates in	470, 471
FMN (flavin mononucleotide)	461
- biosynthesis of cell constituents from	499 sq.
- constituents, degradation	482 sq.
- utilization	472
Formaldehyde, «active», in formation of glycine from serine	507
- in glycine degradation	480
α -L-Formamidinoglutamic acid in L-histidine degradation	478
5-Formamido-4-carboxamidoimidazole ribotide in formation of inosinic acid	510
Formamido-L-glutamic acid. See α -L-Formamidinoglutamic acid	
Formic acid in L-histidine degradation	477, 478
Formylase, glutamine, in L-histidine degradation	478
L-Formylglutamic acid in L-histidine degradation	478
Formylglycinamide ribotide	458
- in formation of inosinic acid	509
Formylglycinamidine ribotide	458
- in formation of inosinic acid	509
Formylkynurenine in tryptophan degradation	482
α -Formylpropionyl-coenzyme A in valine degradation	479
Formyltetrahydrofolic acid in formation of inosinic acid	509, 510
Fructokinase in glycolysis	473
D-Fructose	430, 433
- formation from glucose	499
Fructose 1,6-diphosphatase	495
D-Fructose-1,6-diphosphate	436
- dephosphorylation by phosphatase	515
- enzymic hydrolysis	495
- in breakdown and synthesis of glycogen	515
- in glycolysis	472, 473
- in pentose-phosphate cycle	501
D-Fructose-1-phosphate	436
- enzymic hydrolysis	495
D-Fructose-6-phosphate	436
- glycolysis and hydrolysis of, by phosphatase	499
- in breakdown and synthesis of glycogen	515
- in glycolysis	472, 473
- in pentose-phosphate cycle	500, 501
Fruit sugar. See D-Fructose	
2-(α -L-Fucopyranosido)lactose	441
L-Fucose	432
Fucosidolactose	441

F	page
Fumarase in tricarboxylic acid cycle	473
Fumaric acid (fumarate), from degradation of foods	484
- in formation of adenylic acid	510
- in breakdown and synthesis of glycogen	515
- in formation of inosinic acid	510
- in phenylalanine and tyrosine degradation	481
- in tricarboxylic acid cycle	473, 474
- in biosynthesis of urea	517, 518
Fumarylacetoacetate hydrolase in phenylalanine and tyrosine degradation	481
Fumarylacetoacetic acid in phenylalanine and tyrosine degradation	481
Furanoses	427 sq.

G	page
Galactokinase in glycolysis	473
4'-(β -D-Galactopyranosido)- β -D-glucopyranose. See Lactose	
D-Galactosamine	433
D-Galactosamine-1-phosphate	437
D-Galactose	429, 433
- interconversion with glucose	463, 464, 499
α -D-Galactose-1-phosphate	437
β -Galactosidase	493
β -Galactosides, enzymic hydrolysis	493
Galacto-waldenase in glycolysis	473
α -D-Galacturonic acid	440
Galaheptulose, structure	430
Gastric juice lipase	494
Gastrointestinal tract, enzymes	487 sq.
GDP. See Guanosine diphosphate	
Gentiobiose, enzymic hydrolysis	493
«Glucocorticoids»	505
α -D-Glucofuranose	429
Gluconeogenesis	514, 515
D-Gluconic acid	440
- 6-phosphate	437
β -L-Glucopyranose	429
α -D-Glucopyranose	429, 430
α -D-Glucopyranosido- β -D-fructofuranoside (sucrose)	441
4'-(α -D-Glucopyranosido)- β -D-glucopyranose. See Maltose	
4'-(β -D-Glucopyranosido)- β -D-glucopyranose. See Cellobiose	
D-Glucosamine	434
D-Glucosamine-6-phosphate	437
Glucosaminidases	494
D-Glucose	429, 430, 434
- alcoholic fermentation	473
- basic cell constituents and metabolites from	499 sq.
- interconversion with galactose	463, 464
- lactic acid fermentation	470 sq.
- formation of serine and glycine from	507
- synthesis from noncarbohydrate precursors	514, 515
- uridine diphosphoglucuronic acid from	502
L-Glucose, structure	429
Glucose 6-phosphatase	495
- dephosphorylation of glucose-6-phosphate by	515
β -D-Glucose-1,6-diphosphate	437
α -D-Glucose-1-phosphate	437
- in breakdown and synthesis of glycogen	515
D-Glucose-6-phosphate	437
- dephosphorylation by phosphatase	515
- enzymic hydrolysis	495
- in breakdown and synthesis of glycogen	515
- in glycolysis	472, 473
- oxidation by pentose-phosphate cycle	499 sq.
Glucose-6-phosphate dehydrogenase in pentose-phosphate cycle	501
α -Glucosidases	493
β -Glucosidase	493
β -Glucosides, enzymic hydrolysis	493
Glucuronic acid, formation from glucose	499, 501, 502
β -D-Glucuronic acid	440
β -Glucuronidase	494
Glucuronides, as detoxication products	516
- formation	502
- enzymic hydrolysis	494
Glutaconic acid in lysine degradation	481
L-Glutamic acid (L-glutamate)	447
- formation, from glucose	499
- from L-histidine	477, 478
- from L-hydroxyproline	478
- from α -ketoglutarate	507

G	page
L-Glutamic acid (L-glutamate), cell constituents and metabolites from	508
- decarboxylation	477
- degradation	477
- glutamine formation from	508
- in aspartate regeneration in urea synthesis	518
- in L-citrulline degradation	478
- in glutathione formation	512
- in guanylic acid formation	511
- in inosinic acid formation	509
- in L-proline degradation	478
- in biosynthesis of taurine	512
- β -monoamide. See Glutamine	
- proline and hydroxyproline formation from	507
- reaction with DPN	476
- regeneration in urea synthesis	517, 518
- transamination, with oxaloacetate	476, 477, 499
- with pyruvate	499
L-Glutamic dehydrogenase	476
- in biosynthesis of glutamic acid	499, 507
Glutamic formylase in L-histidine degradation	478
L-Glutamic γ -semialdehyde, in L-citrulline degradation	478
- in biosynthesis of proline and hydroxyproline	507
- in L-proline degradation	478
- in transamination reactions	477
L-Glutamine	447
- conjugation, as detoxication mechanism	516
- formation and function	508
- in formation of guanylic acid	511
- in formation of inosinic acid	509
- in detoxication of phenylacetic acid	519
- transamination	477
γ -L-Glutamyl-L-cysteine in glutathione formation	512
Glutaric acid in lysine degradation	481
Glutathione, formation	512
- function	508
Glyceraldehyde, stereoisomerism	427, 428
D-Glyceraldehyde	428, 429, 432
- 3-phosphate	435
- formation of glucose-6-phosphate from	501
- in 2-deoxyribose-5-phosphate degradation	482
- in breakdown and synthesis of glycogen	515
- in glycolysis	472, 473
- in pentose-phosphate cycle	500, 501
L-Glyceraldehyde	428
D-Glyceric acid	440
- in biosynthesis of glycine and serine	507
- 1,3-diphosphate	435
- in breakdown and synthesis of glycogen	515
- in glycolysis	472
- 2,3-diphosphate	435
- 2-phosphate	435
- in breakdown and synthesis of glycogen	515
- in glycolysis	472
- 3-phosphate	435
- in biosynthesis of glycine and serine	507
- in breakdown and synthesis of glycogen	515
- in glycolysis	472
Glyceride fats. See Fats	
Glycerol	439
- conversion into carbohydrate	475
- in fats, formation of	503
- phosphates, formation from glucose	499
- 1-phosphate, in biosynthesis of lecithin and cephalin	502
L-Glycerol 1-phosphate	435
Glycerophosphates. See Glycerol phosphates	
Glycerophosphate dehydrogenase, in formation of glycerophosphates from glucose	499
Glycerolphosphorylcholine, enzymic hydrolysis	497
Glycerolphosphorylcholine diesterase	497
Glycerolphosphorylethanolamine, enzymic hydrolysis	497
Glycinamide ribotide	458
- in formation of inosinic acid	509
Glycine	447
- cell constituents and metabolites from	508
- conjugation as detoxication mechanism	516
- with aromatic acids	519
- conjugation with bile acids	512
- creatine formation from arginine, methionine and	511
- degradation	480
- formation from glucose	499

- G** page
- Glycine, formation from serine 507
- in glutathione formation 512
- in formation of inosinic acid 509
- in L-threonine degradation 480
- biosynthesis of porphyrins from succinic acid and 511
- residues, enzymic hydrolysis 490, 491
- transamination 477
- Glycocyanine. See Guanidinoacetic acid
- Glycogen 443
- breakdown and synthesis 515
- enzymic hydrolysis 493
- formation from glucose 499
- lactic acid fermentation 473
- Glycolaldehyde, «active», in pentose-phosphate cycle 500
- Glycolysis 470 sq.
- Glycosidases 487, 493, 494
- Glycosides 427
- Glycylglycine dipeptidase 491, 492
- Glycyl-L-histidine, enzymic hydrolysis 492
- Glycyl-L-leucine dipeptidase 491, 492
- Glyoxalase in glycine degradation 480
- Glyoxalate in transamination reactions 477
- GMP (guanosine monophosphate). See Guanylic acid
- Grape sugar. See D-Glucose
- GTP. See Guanosine triphosphate
- Guanase 498
- in guanylic acid degradation 483, 484
- Guanidinoacetic acid 451
- in creatine formation 511
- Guanine 454
- enzymic deamination 498
- degradation 483, 484
- desoxyriboside. See Desoxyguanosine
- in guanylic acid degradation 483
- riboside. See Guanosine
- Guanosine 455
- enzymic deamination 498
- in guanylic acid degradation 483
- monophosphate (GMP). See Guanylic acid
- diphosphate (GDP) 459
- – in formation of adenylic acid 510
- – reaction with succinyl-coenzyme A 486
- diphosphate mannose 463
- triphosphate (GTP) 459
- – formation from GDP and succinyl-coenzyme A 486
- – in phosphorylation of adenosine diphosphate 486
- – in formation of adenylic acid 510
- Guanosine deaminase 484, 498
- Guanylic acid (GMP) 459
- enzymic deamination 498
- degradation 483, 484
- formation 511
- Guanylic deaminase 498
- in guanylic acid degradation 483, 484
- D-Guloheptulose, structure 430
- D-Gulose, structure 429
- H**
- Halogenobenzenes, mercapturic acid formation from 519
- «HARDEN-YOUNG Ester». See D-Fructose-1,6-diphosphate
- HAWORTH formulas 429, 430
- Heart, esterases 495
- glycosidases 494
- phospholipase 496
- Hemiacetals 427
- Hemiketals 427
- Heparin 443
- enzymic hydrolysis 494
- formation 519
- Heparinase 494
- D-*altro*Heptulose 434
- Hexahydrohexahydroxybenzene, isomerism 428
- Hexokinase in glycolysis 472, 473
- Hexoses 433, 434
- Hexose diphosphatase, dephosphorylation of fructose-1,6-diphosphate by 515
- Hexose-phosphate isomerase, in glycolysis 472
- in pentose-phosphate cycle 500, 501
- Hippuric acid, as detoxication product 516
- formation from benzoic acid 519
- function 508
- Histamine, formation from histidine 477
- function 508
- H** page
- Histidase in L-histidine degradation 477
- Histidine 447
- cell constituents and metabolites from 508
- decarboxylation 477
- degradation 477, 478
- Holo-enzymes 467
- L-Homocysteine degradation 480
- in creatine formation 511
- in L-methionine degradation 480
- Homogentisic acid in phenylalanine and tyrosine degradation 481
- Homogentisic oxidase in phenylalanine and tyrosine degradation 481
- L-Homoserine 451
- degradation 479
- in L-homocysteine degradation 480
- Hormones, adrenocortical. See Adrenal steroids
- thyroid. See Thyroid hormone
- Hyaluronic acid 443
- enzymic hydrolysis 494
- Hyaluronidases 494
- Hydrindantin 445
- Hydrocortisone, biosynthesis 504, 505
- Hydrolases, nucleotide 484
- Hydrolase, fumarylacetoacetate, in phenylalanine and tyrosine degradation 481
- β -Hydroxyacyl-coenzyme A in fatty-acid oxidation 475
- β -Hydroxyacyl-dehydrogenase in fatty-acid oxidation 475
- Hydroxyamino acids, degradation 479, 480
- «Hydroxyamino acid aldolase» 480
- 11 β -Hydroxy- Δ^4 -androsterone-3,17-dione, synthesis from cholesterol 504, 505
- 19-Hydroxy- Δ^4 -androsterone-3,17-dione, biosynthesis and metabolism 506, 507
- synthesis from cholesterol 504, 505
- 3-Hydroxyanthranilic acid in tryptophan degradation 481, 482
- β -Hydroxybutyrate in fatty-acid degradation 476
- β -Hydroxybutyric dehydrogenase in fatty-acid degradation 476
- β -Hydroxyisobutyryl-coenzyme A in valine degradation 479
- 17 α -Hydroxydesoxycorticosterone, synthesis from cholesterol 504, 505
- 18-Hydroxydesoxycorticosterone, synthesis from cholesterol 504, 505
- 16 α -Hydroxyestrone, biosynthesis and metabolism 506, 507
- 16 β -Hydroxyestrone, biosynthesis 506, 507
- 18-Hydroxyestrone, biosynthesis 506, 507
- α -Hydroxyglutaric acid in glycine degradation 480
- in lysine degradation 481
- β -Hydroxyglutaric acid in lysine degradation 481
- 5-Hydroxyindoleacetaldehyde in degradation of 5-hydroxytryptamine 514
- 5-Hydroxyindoleacetic acid in degradation of 5-hydroxytryptamine 514
- 8-Hydroxykynurenic acid in tryptophan degradation 481, 482
- 3-Hydroxykynurenine in tryptophan degradation 481, 482
- 8-Hydroxylysine 447
- β -Hydroxy- β -methylglutaric acid in biosynthesis of cholesterol 503
- β -Hydroxy- β -methylglutaryl-coenzyme A in leucine degradation 478
- β -Hydroxy- β -methyl- δ -valerolactone in biosynthesis of cholesterol 503
- p*-Hydroxyphenylpyruvic acid in phenylalanine and tyrosine degradation 481
- 17 α -Hydroxyprogesterone, synthesis from cholesterol 504, 505
- L-Hydroxyproline 447
- biosynthesis 507
- degradation 478
- formation from glucose 499
- function 508
- γ -Hydroxyproline- α -carboxylic acid. See L-Hydroxyproline
- Hydroxypyruvic acid in biosynthesis of glycine and serine 507
- in transamination reactions 477
- 5-Hydroxytryptamine (serotonin), formation and degradation 514
- formation from 5-hydroxytryptophan 477
- function 508
- 5-Hydroxytryptophan, decarboxylation 477
- 5-hydroxytryptamine formation from 514
- H** page
- β -Hydroxyisovaleric acid in biosynthesis of cholesterol 503
- β -Hydroxy-*n*-valeryl-coenzyme A in norleucine degradation 479
- β -Hydroxyisovaleryl-coenzyme A in leucine degradation 478
- Hypotaurine in biosynthesis of taurine 512
- Hypoxanthine 454
- degradation 483, 498
- desoxyriboside 451
- in adenylic acid degradation 484
- riboside. See Inosine
- I**
- D-Idose, structure 429
- IDP (inosine diphosphate) in CO₂-fixation by phosphopyruvate 502, 515
- D-Iduronic acid 440
- Imidazolonepropionic acid in L-histidine degradation 478
- Imidodipeptidase 491, 492
- α -Iminobutyric acid in homoserine degradation 480
- Iminodipeptidase 491, 492
- α -Iminopropionic acid, in L-cysteine and cysteine degradation 480
- in serine degradation 479
- IMP. See Inosinic acid
- Inosine 456
- in adenylic acid degradation 484
- diphosphate (IDP) in CO₂-fixation by phosphopyruvate 502, 515
- 5'-monophosphate (IMP). See Inosinic acid
- triphosphate (ITP) in CO₂-fixation by phosphopyruvate 502, 515
- Inosinic acid (IMP) 458
- formation 509
- enzymic hydrolysis 498
- in adenylic acid degradation 483
- in adenylic acid formation 510
- in xanthidyllic acid formation 511
- Inosinic oxidase in adenylic acid degradation 483
- meso*Inositol 439
- myo*-Inositol 439
- Intestine, esterases 495, 496
- lipase 494
- mucosa, esterases 495
- – fermentation and respiration rates in 470, 471
- nucleases 498
- small, exopeptidases 491
- – glycosidases 493
- – proteases 489
- Inulin 444
- Iodobenzene, mercapturic acid formation from 519
- S-p*-Iodophenylcysteine 519
- p*-Iodophenylmercapturic acid 519
- Iris, glycosidases 494
- Iron porphyrins, electron transport in, in cells 485
- fate of, in body 482
- Isodulcitol 432
- Isoleucine. See *iso*Leucine
- Isomerase, cis-trans-, in phenylalanine and tyrosine degradation 481
- hexose-phosphate, in glycolysis 472
- pentose-phosphate, in pentose-phosphate cycle 500
- triose-phosphate, in glycolysis 472
- Isopentane in biosynthesis of cholesterol 503
- Isoprene in biosynthesis of cholesterol 503
- ITP. See Inosine triphosphate
- J**
- Jejunum, lipase 494
- JENSEN's sarcoma, fermentation and respiration rates in 470, 471
- K**
- Ketals 427
- β -Ketoacyl-coenzyme A in fatty-acid oxidation 475
- β -Ketoacyl-thiolase in fatty-acid oxidation 475
- α -Ketoadipic acid in lysine degradation 481
- α -Keto- ϵ -amino adipic acid in lysine degradation 480
- α -Keto- δ -amino-*n*-valeric acid in D-ornithine degradation 478
- γ -Keto- δ -amino-*n*-valeric acid. See δ -Amino-levalulinic acid

K	page
2-Keto-D-arabohexose. See D-Fructose	
α -Ketobutyric acid in homoserine degradation	480
α -Ketocaproic acid in norleucine degradation	479
16-Ketoestradiol, biosynthesis and metabolism	506, 507
16-Ketoestrone, biosynthesis and metabolism	506, 507
α -Ketoglutaric acid (α -ketoglutarate), formation, from degradation of foods	484
— from L-glutamic acid	476, 477
— biosynthesis of L-glutamic acid from	507
— in aspartate regeneration in urea synthesis	518
— in glutamate regeneration in urea synthesis	518
— in glycine degradation	480
— in lysine degradation	481
— in tricarboxylic acid cycle	473, 474
— transamination reactions	476, 477
— transamination with β -alanine	482
— in biosynthesis of taurine	512
α -Ketoglutaric dehydrogenase in tricarboxylic acid cycle	473
α -Ketoglutaric semialdehyde in glycine degradation	480
α -Keto- γ -guanidinovaleic acid in transamination reactions	477
D- <i>altro</i> Ketoheptose	434
Ketohexokinase in glycolysis	473
α -Keto- β -methylvaleric acid, in isoleucine degradation	479
Ketone bodies (acetone bodies)	475, 476
α -Ketonic acids, formation from α -amino acids	476
— oxidation	474
3-Keto-6-phosphogluconic acid in pentose-phosphate cycle	500, 501
Ketoses	427, 428
Ketosis	475, 476
17-Ketosteroids, excretion	505
D-Keto-sugars, configurational relationships	430
α -Ketoisovaleric acid, in leucine degradation	478
— in valine degradation	479
β -Ketovaleryl-coenzyme A in norleucine degradation	479
Kidney, amino acid degradation in	477 sq.
— amino acid oxidases	476
— cortex, fermentation and respiration rates in	470, 471
— esterases	495
— glycosidases	493, 494
— medulla, fermentation and respiration rates in	470, 471
— nucleases	498
— phospholipase	496
— proteases	491, 492
— transamination reactions in	477
«KIESSLING Ester». See D-Glyceric acid 2-phosphate	
Kinase, adenylate, in biological energy transformations	486
— pyruvate, in glycolysis	472
KREBS cycle. See Tricarboxylic acid cycle	
Kynurenine acid in tryptophan degradation	481, 482
Kynurenine in tryptophan degradation	481, 482
L	
Lacrimal secretion, glycosidases of	494
Lactic acid (lactate), conversion to pyruvate	473
— in breakdown and synthesis of glycogen	515
Lactic acid fermentation	470 sq.
Lactic dehydrogenase in glycolysis	472
«Lactonase», in pentose-phosphate cycle	500
Lactose	441
— formation from glucose	499
Lactose-phosphate	438
Lanosterol in biosynthesis of cholesterol	503
Lecithin, biosynthesis	502
— enzymic hydrolysis	496, 497
Lecithinases	496, 497
L-Leucine	448
— degradation	478
— enzymic hydrolysis	491
L-Leucine residues, enzymic hydrolysis	490, 491
isoLeucine	448
— degradation	479
— residues, enzymic hydrolysis	490
L-Leucine aminodipeptidase	491, 492
Levulose. See D-Fructose	
Lipases	487
— gastrointestinal	494
— pancreatic	494

L	page
α -Lipoic acid, in pyruvate oxidation	474
— in tricarboxylic acid cycle	473
Liver, amino acid degradation in	477 sq.
— amino acid oxidases	476
— esterases	495, 496
— fermentation and respiration rates	470, 471
— glycosidases	493, 494
— nucleases	498
— phospholipase	496
— proteases	491, 492
— transamination reactions	477
Liver starch. See Glycogen	
Lung, esterases	495
— fermentation and respiration rates	470, 471
— glycosidases	494
— nucleases	498
— proteases	492
Lymphoid tissue, esterases	495
L-Lysine	448
— decarboxylation	477
— degradation	480, 481
— formation from α , ϵ -diaminopimelic acid	477
— residues, enzymic hydrolysis	489
Lysolipids, formation from phospholipids	496
Lysophosphatides, enzymic hydrolysis	497
Lysozyme	494
D-Lyxoketose. See D-Xylulose	
L-Lyxoketose	433
D-Lyxose, structure	429
D-Lyxulose, structure	430
L-Lyxulose	433

M	page
Maleylacetoacetic acid in phenylalanine and tyrosine degradation	481
L-Malic acid (L-malate), in aspartate regeneration in urea synthesis	518
— in carbohydrate synthesis	515
— in breakdown and synthesis of glycogen	515
— in CO ₂ -fixation by pyruvate	502
— in phenylalanine and tyrosine degradation	481
— in tricarboxylic acid cycle	473, 474
Malic dehydrogenase, in carbohydrate synthesis	515
— in tricarboxylic acid cycle	473
Malic enzyme in carbohydrate synthesis	502, 515
Malonic semialdehyde, from β -alanine	482
— in transamination reactions	477
Malt sugar. See Maltose	
Maltase	493
Maltose	441
— enzymic hydrolysis	493
isoMaltose, enzymic hydrolysis	493
Mammary gland, esterases	495
D-Mannoheptulose, structure	430
D-Mannose	429, 434
D-Mannose-6-phosphate	437
Melanin, formation from tyrosine	514
Menthol, detoxication in body	516
Menthylglucuronide as detoxication product	516
Mercapturic acids, formation, as detoxication mechanism	516, 519
Mesoinositol	439
Metabolic quotients	470
Metabolism	470 sq.
— inborn errors of	481
Metaphosphatases	487
L-Methionine	448
— cell constituents and metabolites from	508
— creatine formation from arginine, glycine and	511
— degradation	480
— in choline formation from serine	508
— residues, enzymic hydrolysis	490
2-Methoxyestrone, biosynthesis	506, 507
α -Methylacetoacetyl-coenzyme A in isoleucine degradation	479
Methylacrylyl-coenzyme A in valine degradation	479
α -Methyl- β -alanine. See β -Aminoisobutyric acid	
Methylation as detoxication mechanism	516
α -Methylbutyryl-coenzyme A in isoleucine degradation	479
α -Methylcarbamyl- β -alanine in thymine degradation	484
3-Methylcrotonic acid in biosynthesis of cholesterol	503
5-Methylcytosine	454
N-Methyl-L-glucosamine	434

M	page
3-Methylglutaconic acid in biosynthesis of cholesterol	503
1-Methylglycocyanidine (creatinine)	451
Methylglycocyanine. See Creatine	450
α -Methyl- β -hydroxybutyryl-coenzyme A in isoleucine degradation	479
Methylmalonyl-coenzyme A, in fatty acid oxidation	475
— in valine degradation	479
N-Methylnicotinamide as detoxication product	516
«Mevalonic acid» in biosynthesis of cholesterol	503
MICHAELIS constant	467 sq.
<i>Micrococcus lysodeikticus</i> , mucopolysaccharides, enzymic hydrolysis	494
Microorganisms, alcoholic fermentation by	470, 473
— respiration and fermentation by	471
Milk, esterases	495
— human, oligosaccharides	441
— nucleases	498
Milk sugar. See Lactose	
«Mineralocorticoids»	505
Molds, threonine degradation by	480
3-Moniodotyrosine	448
— in formation of thyroid hormones	514
Monosaccharides	427 sq.
— of importance to mammals	432 sq.
Mucopolysaccharides, enzymic hydrolysis	494
— synthesis	465
Mucosa, intestinal. See under Intestine	
Mucus, glycosidases	494
Muscle, creatine-ATP reaction	512
— esterases	495
— glycosidases	493
— lactic acid production	471
— nucleases	498
— phospholipase	496
— proteases	492
— respiration rates	470
Myo-inositol	439
Myokinase in biological energy transformations	486
N	
Naphthalene, detoxication in body	516, 519
— mercapturic acid formation from	519
Naphthylmercapturic acid, as detoxication product	516
Nerves, esterases	495
«NEUBERG Ester». See D-Fructose-6-phosphate	
Nicotinamide, detoxication in body	516
— mononucleotide (NMN)	460
— enzymic hydrolysis	498
Nicotinic acid, formation and function	508
— in tryptophan degradation	481, 482
Ninhydrin	445
Ninhydrin reaction	445
NMN. See Nicotinamide mononucleotide	
Noradrenaline, formation from tyrosine	513
— function	508
Norepinephrine. See Noradrenaline	
Norleucine	448
— degradation	479
Norvaline, degradation	479
Nucleases	497, 498
Nucleic acids	452, 453
— enzymic hydrolysis	496, 498
Nucleosides	452, 455 sq.
— enzymic degradation	484, 498
— nomenclature	453
— phosphates. See Nucleotides	
Nucleoside phosphorylases	484, 498
— in adenylic acid degradation	483
— in guanylic acid degradation	483
— in purine metabolism	483
5'-Nucleotidase	498
— in adenylic acid degradation	483
— in guanylic acid degradation	483
— in purine metabolism	483
Nucleotides (See also Ribonucleotides), and related substances	452 sq.
— enzymic degradation	484
— nomenclature	453
— purine and pyrimidine, synthesis and breakdown	454 sq.
— pyridine, as enzyme prosthetic groups	485
— with coenzyme functions	460 sq.
— without coenzyme functions	458
Nucleotide hydrolases	448

P	page
Prostate, esterases	493
Prosthetic groups. See Coenzymes	
Proteases	487 sq., 491, 492
— precursors	488 sq.
Proteinases. See Proteases	
Proteins, amino acid components	446 sq.
— peptic hydrolysis	488
Proteolytic enzymes. See Proteases	
Protoporphyrin 9	511
Pregnenolone, synthesis from cholesterol	504, 505
Progesterone, synthesis from cholesterol	504, 505
Prunasin, enzymic hydrolysis	493
<i>Pseudomonas fluorescens</i> , L-histidine degradation in	478
Psicose, structure	430
Purine	452
— 6-amino-. See Adenine	
— 2-amino-6-hydroxy-. See Guanine	
— 2,6-dihydroxy-. See Xanthine	
— 6-hydroxy-. See Hypoxanthine	
— 2,6,8-trihydroxy-. See Uric acid	
Purine bases, degradation	482 sq.
— formation from amino acids	509 sq.
— function	508
— enzymic hydrolysis and oxidation	484
Purine nucleotides. See under Nucleotides	
Purine oxidases	484
Putrescine, formation from ornithine	477
Pyranoses	428 sq.
Pyridine	452
Pyridine nucleotides. See under Nucleotides	
Pyridoxal phosphate in decarboxylases and transaminases	477
Pyrimidine	452
— 6-amino-2-hydroxy-. See Cytosine	
— 4-carboxy-2,6-dihydroxy-. See Orotic acid	
— 2,6-dihydroxy-. See Uracil	
— 2,6-dihydroxy-5-methyl-. See Thymine	
Pyrimidines, degradation	482 sq.
— formation	513
— function	508
Pyrimidine nucleotides. See under Nucleotides	

- in biosynthesis of urea	517
- inorganic	496
Pyrophosphates, enzymic hydrolysis	496
Pyrophosphate bonds in biological energy transformations	486
Pyrophosphorylase in glycolysis	473
1-Pyrophosphorylribose-5-phosphate. See D-Ribose-5-phosphate-1-pyrophosphate	
Pyrrolidine- α -carboxylic acid. See L-Proline	
L- Δ^1 -Pyrroline-5-carboxylic acid, in L-proline degradation	478
- in biosynthesis of proline and hydroxyproline	507
Pyruvate kinase in glycolysis	472
Pyruvic acid (pyruvate), CO ₂ -fixation by	502
- enol phosphate. See Phosphopyruvic acid	
- formation, from L-alanine	477
- - from lactate	473
- in alcoholic fermentation	473
- in L-cysteine and cystine degradation	480
- in breakdown and synthesis of glycogen	514, 515
- in glycolysis	472
- in biosynthesis of taurine	512
- reaction with thiamine pyrophosphate	474
- transamination reactions	477
- transamination with glutamate	499
R	
Racemates	428
Red blood cells. See Erythrocytes	
Rennin	488
Respiratory rates in tissues	470, 471
Retina, avian, lactic acid production in	471
- fermentation and respiration rates in	470, 471
L-Rhamnose	432
Ribitol	439
D-Ribofuranose. See D-Ribose	
Ribonucleases	487, 488, 497
Ribonucleic acids (RNA)	452, 453
- enzymic cleavage	487, 488, 497
Ribonucleotides (<i>See also Nucleotides</i>)	453
D-Ribose	429, 433
D-Ribose-1,5-diphosphate	436
α -D-Ribose-1-phosphate	435
- in adenylic acid degradation	483
- in guanylic acid degradation	483
- in purine metabolism	483

R	page
D-Ribose-5-phosphate	435
- formation from glucose	499
- in formation of inosinic acid	509
- in pentose-phosphate cycle	500, 501
D-Ribose-5-phosphate-1-pyrophosphate	436
- in formation of inosinic acid	509
- in biosynthesis of pyrimidines	513
Ribosides	453
Riboside diphosphates	453
Riboside monophosphates	453
Riboside triphosphates	453
Ribosylamine-5-phosphate	458
- in formation of inosinic acid	509
Ribotides	453
D-Ribulose	430, 433
D-Ribulose-5-phosphate	436
- in pentose-phosphate cycle	500, 501
RNA. See Ribonucleic acids	
«ROBISON Ester». See D-Glucose-6-phosphate	
«ROBISON-TANKO Ester». See D-Fructose-1-phosphate	
Rous sarcoma, fermentation and respiration rates in	470, 471

S

Saccharic acids	431
Saccharose (sucrose)	441
Salicin, enzymic hydrolysis	493
Saliva, esterases	495
- glycosidases	493
- lipase	494
Sarcosine residues, enzymic hydrolysis	491
Sarcosyl-L-leucine, enzymic hydrolysis	491
Scorpion venom, phospholipase of	496
D-Sedoheptulose	430, 434
D-Sedoheptulose-1,7-diphosphate	438
D-Sedoheptulose-7-phosphate	438
- in pentose-phosphate cycle	500, 501
Semen, glycosidases	494
- nucleases	498
Seminose. See D-Mannose	
Seneciyl-coenzyme A in leucine degradation	478
Seneciyl-hydrazine in leucine degradation	478
L-Serine	448
- cell constituents and metabolites from	508
- decarboxylation	477
- degradation	479
- formation, from carbohydrate	507
- from glucose	499
- in glycine degradation	480
- in L-homocysteine degradation	480
- transamination	477
Serine dehydrase, in serine degradation	479
Serotonine. See 5-Hydroxytryptamine	
Serum, proteases	492
Serratia species, phospholipase of	497
Skin, esterases	495
- fermentation and respiration rates	470, 471
Snake venoms, enzymes	496
D-Sorbose, structure	430
L-Sorbose-1,6-diphosphate, enzymic hydrolysis	495
Sperm. See Semen	
Sphingomyelins, enzymic hydrolysis	497
Spleen, esterases	495, 496
- fermentation and respiration rates	470, 471
- glycosidases	494
- nucleases	497, 498
- proteases	491, 492
Squalene in biosynthesis of cholesterol	503
Starch	444
- A- and B-fractions	442
- enzymic digestion	493
- lactic acid fermentation	473
- liver. See Glycogen	
Steapsin (pancreatic lipase)	494
Stereoisomerism	427
Steroids, adrenocortical. See Adrenal steroids	
- estrogenic. See Estrogens	
- formation from glucose	499
- sulfates, formation	519
Sterols, formation from glucose	499
Stomach, esterases	495
- lipase	494
- proteases	488
Streptidine	439
Submaxillary gland, fermentation and respiration rates in	470, 471

S	page
Succinic acid (succinate), formation, from degradation of foods	484
- from propionyl-coenzyme A	475
- in fatty-acid degradation	476
- in isoleucine degradation	479
- in tricarboxylic acid cycle	473, 474
- in valine degradation	479
- formation of porphyrins from glycine and	511
Succinic dehydrogenase in tricarboxylic acid cycle	473
Succinic semialdehyde in transamination reactions	477
Succinyladenylic acid (succinyladenosine 5'-phosphate)	458
Succinyl-coenzyme A, in fatty-acid degradation	476
- in glycine degradation	480
- in biosynthesis of porphyrins	511
- in tricarboxylic acid cycle	473, 474
- reaction with GDP	486
Sucrose	441
Sugars, D-aldo-, configurational relationships	429
- D-keto-, configurational relationships	430
- phosphates	430, 431, 435 sq.
See also Carbohydrates	
Sulfanilamide, acetylation	518
- detoxication in body	516
Sulfatases	487
Sulfate esters, as detoxication products	516
β-Sulfinylpyruvic acid in biosynthesis of taurine	512
Sulfomucases	494
Sulfuric acid esters, formation	519

T

D-Tagatose, structure	430
D-Talose, structure	429
Tartaric acid, isomerism	428
Taurine	451
- conjugation with bile acids	512
- formation, from cysteic acid	477
- from cysteine	512
- function	508
Testes, fermentation and respiration rates in	470, 471
- glycosidases	494
Testosterone, biosynthesis and metabolism	506
Tetraethyl pyrophosphate, inhibition of choline esterases by	495
Tetrahydrofolic acid in formation of inosinic acid	509, 510
3, 5, 3', 5'-Tetraiodothyronine. See Thyroxine	
Tetroses	432
Thiamine pyrophosphate (TPP), in pentose-phosphate cycle	500
- in tricarboxylic acid cycle	473
- reaction with pyruvate	474
Thioctic acid. See α-Lipoic acid	
«Thiokinases» in fatty-acid oxidation	474
Thiolhistidine betaine (ergothioneine)	451
«Thiopherase» in fatty-acid degradation	476
L-Threonine	449
- degradation	480
- in homoserine degradation	479
D-Threose, structure	429
Thrombocytes, fermentation and respiration rates in	470, 471
Thymine	454
- degradation	484
- desoxyriboside. See (Desoxy)thymidine	
Thymine. See 2-Desoxy-D-ribose	
Thymus, fermentation and respiration rates in	470, 471
- nucleases	497
Thyroglobulin, amino acids	446, 448, 449
- formation	514
- thyroid, iodide concentration by	514
- respiration rates in	470
Thyroid hormone. See Thyroglobulin	
Thyronine, 3, 5, 3'-triiodo-	449
- 3, 5, 3', 5'-tetraiodo-. See Thyroxine	
Thyroxine	449
- formation	514
- function	508
Tiglyl-coenzyme A, in isoleucine degradation	479
Tissues, CO ₂ fixation in	502
- fermentation and respiration rates in	470, 471

TPN (triphosphopyridine nucleotide)	460
- in carbohydrate synthesis	515
- in CO ₂ -fixation by pyruvate	502
- in glutamate regeneration in urea synthesis	518
- in pentose-phosphate cycle	500, 501
- in tricarboxylic acid cycle	473
- reduced, in biosynthesis of glutamic acid	507
- in breakdown and synthesis of glycogen	515
TPNH, TPNH ₂ . See TPN, reduced	
TPP. See Thiamine pyrophosphate	
Transaldolase in pentose-phosphate cycle	500, 501
Transaminases	477
Transamination	476, 477
Transketolase in pentose-phosphate cycle	500, 501
Tricarboxylic acid cycle	473, 474, 484, 485
3, 5, 3'-Triiodothyronine	449
- formation	514
Triketohydrindene	445
- hydrate	445
«Triokinase»	475
- in glycolysis	473
Trioses	432
Triose-phosphate dehydrogenase in glycolysis	472
Triose-phosphate isomerase in glycolysis	472
Tripeptidase	491, 492
Tripeptides, enzymic hydrolysis	491
Triphosphopyridine nucleotide. See TPN	
Trypsin	489
- action on procarboxypeptidase	490
Trypsinogen	489
Tryptophan	449
- cell constituents and metabolites from	508
- degradation	481, 482
- 5-hydroxytryptamine formation from	514
- residues, enzymic hydrolysis	490
Tyramine, formation from tyrosine	477
L-Tyrosine	449
- adrenaline and noradrenaline formation from	513
- cell constituents and metabolites from	508
- decarboxylation	477
- degradation	481
- 3, 5-diiodo-	446
- in formation of thyroid hormones	514
- melanin formation from	514
- 3-monoiodo-. See 3-Monoiodotyrosine	
- residues, enzymic hydrolysis	488, 490
Tyrosinosis	481

U

UDP. See Uridine diphosphate	
UMP (Uridine monophosphate). See Uridylic acid	
Uracil	454
- degradation	482, 484
- riboside. See Uridine	
Urea, biosynthesis	516 sq.
- degradation	484
Urea cycle	517, 518
Ureidosuccinic acid. See Carbamylaspartic acid	
Uric acid	454
- enzymic oxidation	498
- in purine metabolism	483, 484
- riboside	457
Uricase	498
- in purine metabolism	483, 484
Uridine	456
Uridine diphosphate (UDP)	459
- N-acetylgalactosamine	465
- N-acetylglucosamine	464
- as detoxication product	516
- galactose	464
- in formation of lactose from glucose	499
- glucosamine	464
- glucose	463
- glucuronic acid	465, 502
Uridine monophosphate. See Uridylic acid	
Uridine triphosphate (UTP)	459
- in biosynthesis of pyrimidines	513
Uridylic acid (uridine monophosphate, UMP)	459
- enzymic hydrolysis	498
- in biosynthesis of pyrimidines	513
Uridyl-transferase in glycolysis	473
Urine, N-acetylcysteine derivatives in	446
Urocanase in L-histidine degradation	477
Urocanic acid in L-histidine degradation	477
Uronic acids	431, 440
- fate of, in body	482
Uterus, proteases	492

U	page
UTP. See Uridine triphosphate	
UTTER-KURAHASHI enzyme in carbohydrate synthesis	515

V	
Valeryl-coenzyme A in norleucine degradation	479
<i>iso</i> Valeryl-coenzyme A in leucine degradation	478
Valine	449
- degradation	479
Venom phospholipases	496
Vitamin-C	440
Vitamin E in biological oxidations	485
Vitamin K in biological oxidations	485
Volemos, structure	430

W	
Wasp venom phospholipase	496
White blood cells. See under Blood cells	

X	page
Xanthidylic acid (xanthosine monophosphate, XMP)	458
- formation	511
- in formation of guanylic acid	511
- in purine metabolism	483
Xanthine	454
- degradation	483
- desoxyriboside. See Desoxyxanthosine	
- enzymic oxidation	498
- in purine metabolism	483
- riboside. See Xanthosine	
Xanthine oxidase	498
- in adenylic acid degradation	484
- in purine metabolism	483
Xanthosine	457
- in purine metabolism	483
Xanthosine 5'-monophosphate (XMP). See Xanthidylic acid	
«Xanthurenic acid» in tryptophan degradation	481, 482

X	page
XMP. See Xanthidylic acid	
L-Xyloascorbic acid	440
D-Xyloketose. See D-Xylulose	
L-Xyloketose	433
D-Xylose, structure	429
D-Xylulose	430, 433
L-Xylulose	433
D-Xylulose-5-phosphate	436
- in pentose-phosphate cycle	500, 501
Xylulo-waldenase, in pentose-phosphate cycle	501

Z	
Zymohecase. See Aldolase	
Zymosterol, in biosynthesis of cholesterol	503
Zwitterions	445

General Index



Note that this index does not include the Supplement (pages 427-519).

This has been separately indexed on pages 520-528.

Anaemia

The following special indexes are also available:

Symbols and abbreviations for units page 50

Names and symbols of the elements page 83

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

A	page	A	page	A	page
α (alpha-particle). See Alpha-particles		Adenosine, in plasma	318	Allyl isothiocyanate, chemical data	103
ac. (acre)	53	- triphosphate, in whole blood	318	Aloes, Aloin, posology	369
ash (apostilb)	72	- - phosphorus, in blood	326	Alphabet, Greek	7
at (technical atmosphere)	60	Adenosinepolyphosphatase, in plasma	324	Alpha rays, biological activity	71
atm (physical atmosphere)	61	Adenylic acid, in plasma	318	- constants	80
A (ampere)	65, 67	ADIE's syndrome	359	Altitude, and haemoglobin content of erythrocytes	337
A (acre)	53	Adiposity, and growth hormone	193	Aluminium, in blood	329
Å (angström)	52	Adiuretin	194	- in organs	282
A ₁ , A ₂ , vitamins	209	Adonis, posology	369	- properties and isotopes	85
Abbreviations and symbols of units	50	Adrenals, chemical composition	282	Amanita poisoning	425
Abdominal circumference during growth	257 sq.	Adrenal cortex, activity and morphological changes	185	Amaurosis. See Blindness	
Abducens pareses	355, 365	- stimulation by ACTH	183	Amebae. See Amoebae	
ABO blood group system	344	Adrenal medulla, and adrenaline	205, 206	Americium, properties and isotopes	97
Abortifacients, poisoning	422	Adrenaline	205 sq.	Amethopterin	220
Absolute electrical units	64	- and eosinopenia	189, 206	Amidone. See Methadone	
- temperature scale	56	- and pituitary	184	Amido-nitrogen, of plasma proteins	315
- zero temperature	56	- posology	369, 402	Amidopyrine, chemical data	103
Abundance. See Natural abundance		Adrenochrome	205	- poisoning	422
Acceleration, angular	59	Adrenocortical hormones. See Corticosteroids		- posology	369, 403
- due to gravity	79	Adrenocorticotrophic hormone (ACTH)	182 sq.	Aminoacetic acid. See Glycine	
- units	59	Adrenogenital syndrome, and urinary steroids	183	Amino-acids	224, 225
Accommodation (eye)	357	Adrenolutine	205	- in aqueous humour (eye)	363
- and depth of anterior chamber	362	Adrenosterone	196	- in breast milk	228, 229
Acedicon, children's doses	402	Actiane, structure and derived steroids	196	- in cerebrospinal fluid	353
Acetanilide, chemical data	103	Actianediolone	196	- essential	224, 225
- posology	368	Actianolone	196, 198	- of food proteins	225
Acetarsol and sodium derivative, posology	368	- in urine	200	- in plasma, free	317
Acetic acid, chemical data	104	9(11)-Actienolone	196	- of plasma proteins	315
- solutions, specific gravity	108	Aetiocholane. See Actiane		- in spermatozoa	277
- test for urinary proteins	294	Afibrinogenaemia	316	- in urine	288, 289
Acetoacetic acid, conversion factor to acetone	126	Agaracin, posology	369	D-Amino-acid oxidase	216
- in plasma	322	Age, and ABO agglutinin titre	342	p-Aminobenzoic acid	219
- in urine	289	- and accommodation (eye)	357	L(+)- α -Aminobutyric acid	224
Acetone, conversion factors to other acetone bodies	126	- and basal metabolism	248	p-Aminhippurate clearance, renal	300
Acetone bodies (See also Acetoacetic acid, β -H-droxybutyric acid)		- and blood pH	308	Aminophylline, chemical data	103
- in blood	322	- and eye-chamber volume	362	- posology	369, 403
- and insulin deficiency	207	- and lens specific gravity (eye)	363	Aminopterin	220
- in urine	289	- and plasma glucosamine	320	4-Aminopteroylaspartic acid	220
- tests for	294	- and plasma iron	330	4-Aminopteroylglutamic acid	220
Acetophenetidin. See Phenacetin		- and plasma polysaccharides	320	Aminopyrine. See Amidopyrine	
Acetyl-p-aminophenyl salicylate, posology	368	- and plasma protein-bound iodine and cholesterol	329	p-Aminosalicic acid, posology	389
Acetylcholine, chemical data	103	- and pupillary diameter	357	Ammonia, chemical data	104
- effect on pupil	357	- and visual defects	357, 364	- conversion factor to ammonia nitrogen	126
- in plasma	318	- and vital capacity	251	- in lacrimal secretion	362
- poisoning	422	Agglutinins (blood grouping)	341 sq.	- nitrogen, conversion factor to ammonia	126
- posology	368, 402	AHLFELD and HAASE, rule of	267	- poisoning	422
Acetylphenetidin. See Phenacetin		L(+)-Alanine	224, 225	- solutions, specific gravity	110
Acetylsalicic acid, chemical data	103	- in plasma	317	- in urine	288
- poisoning	426	- of plasma proteins	315	Ammonium chloride, chemical data	104
- posology	368, 402	β -Alanine	224	- electrolytic data	118-120
Achlorhydria	285, 286	Albumins, amino-acid composition	315	- isotonic solution	125
Achloropsia (test charts inside back cover)		- in cerebrospinal fluid	352, 353	- poisoning	422
Acids, excess, in foods	231 sq.	- and colloid-osmotic pressure of blood	296, 305	- hydroxide, chemical data	104
- fatty. See Fatty acids		- electrophoretic mobility	309	- magnesium phosphate, in urinary sediments	292, 293
- free, of gastric juice	284 sq.	- in lens (eye)	363	- salts, chemical data	104
- poisoning	422	- in pancreatic juice	283	- posology	369, 403
Acid-base indicators	106	- plasma and serum	313 sq.	Amodiaquine, posology	161, 370
- relationships in serum	297	- in pregnancy	273	Amoebae (See also Pathogen index, page 172) 157 sq.	
Acid-formers in blood	297, 326	- in urine	288	- classification	171
Acidity (gastric juice)	284 sq.	Albuminuria	288	Amoebiasis	157
Acidosis, definition	297	Alcohol. See Ethyl alcohol		Ampere	64
- infusion therapy	122 sq.	Alcohols, poisoning	422	Amphetamine, chemical data	103
Aconite, poisoning	422	Aldehyde oxidase	216	- in barbiturate poisoning	423
- posology	368	Aldolase, in plasma	324	- posology	370
Aconitine, chemical data	103	Aldosterone	203	Amyl alcohol, poisoning	422
- poisoning	422	Alizarin yellow, indicator range	106	Amyl nitrate, blood circulation time measured with	301
- posology	369	Alkalis, poisoning	422	- nitrite, chemical data	103
Acoustic units	73	Alkali loading test	288	- posology	370, 403
Acromegaly	193	Alkali reserve	297, 330, 331	Amylase, in plasma	324
ACTH (corticotropin)	182 sq.	- in acidosis and alkalosis	297	- in urine	290
- children's doses	402	- determination	330	Amylene hydrate, posology	370
Actinium, properties and isotopes	95	Alkaloids, international standards	79	Amylocaine, posology	370
Actinium-A, -B, -C, -C'	94	Alkalosis, definition	297	Anaemia (See also Disease index, page 172)	
Actinium-C"	93	- infusion therapy	122 sq.	- deficiency	220-222
Actinium-K and -X	95	Alkaptonuria	290	- goat's milk	220-222
Actinium-U	96	Alkyl phosphates, effect on pupil	357	- iron-deficiency	330
Actinon (actinium emanation)	95	Alkylsulphuric acids, in urine	290	- macrocytic, and vitamin B ₁₂	221, 222
Action units	62	Allantoin, in plasma	318	- megaloblastic	220-222
Acusticus neurinoma, and ocular symptoms	366	- in urine	288	- pernicious, and gastric juice	286
Adaptation (eye)	358	Allobarbitone, posology	369	- and leucocyte distribution	340
Addenda and errata	4	Allonal, children's doses	402	- and vitamin B ₁₂	221, 222
ADDISON's disease, and 17-ketosteroids in urine	183	Allopregnane, structure and derived steroids	196	- and plasma porphyrins	338
- therapy	189	isoAlloxazine	215	- of pregnancy	220-222
		Allyl alcohol, poisoning	422	- and reticulocytes	334
		N-Allylnormorphine, as antidote for opiates	425		

Note that this index does not include the Supplement (pages 427-519).
This has been separately indexed on pages 520-528.

Analysis

The following special indexes are also available:

Symbols and abbreviations for units page 50

Names and symbols of the elements page 83

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

A	page
Analysis, conversion factors in	126
- correction of gas volumes in	127
- units	75, 76
Analytical units	75, 76
Androgens	196, 201
- function	204
- metabolism	197, 198
Androstane, structure and steroid derivatives	196
Androstanediol	196
Androstanedione	196
4-Androstenedione, chemistry	196
- metabolism	198
9(11)-Androstenedione	196
Androsterone	201
- chemistry	196
- metabolism	198
<i>epi</i> Androsterone	196
Anemia. See Anaemia	
Anerythrospia (test charts inside back cover)	
Aneurine. See Vitamin B ₁	
Angina, PLAUT-VINCENT	141, 148
Angle units	57
Ångström unit	52
Angular acceleration	59
- momentum, BOHR's unit	81
- velocity	59
Anhydrohydroxyprogesterone	196
Aniline, poisoning	422
Animal protein factor. See Vitamin B ₁₂	
Anions, in blood	297, 326
- definition	115
- in various electrolytes	118-120
- in urine	290, 299
Anisocytosis	336
Annus fictus	56
Anomalous year	56
ANSELMINO and HOFFMANN's hormone of carbohydrate metabolism	181
Antiadrenergics and ACTH secretion	184
- and gonadotropin secretion	180
- effect on pupil	357
Antibiotics, and infectious diseases	128 sq.
- international standards	79
Antibodies, of blood groups	341 sq.
Anticholinergics, and gonadotropin secretion	180
- effect on pupil	357
Antidysentery serum. See under Dysentery	
Antifebrin. See Acetanilide	
Antigens, of blood groups	341 sq.
- international standards	78
Antigen-antibody reaction	341
- and ACTH	188
Antihistamines, children's doses	403
Anti-human globulin solution, in blood grouping	341
Antilogarithms	6, 7
Antimalarials	161
Antimonials, posology	370
Antimony, properties and isotopes	89
- potassium tartrate. See Tartar emetic	
Anti-pernicious anaemia factor. See Vitamin B ₁₂	
Antipyrine. See Phenazone	
Antisera, international standards	77
Antithyroid substances	208
Antitoxins, international standards	77
APF (Animal protein factor). See Vitamin B ₁₂	
Apiol, poisoning	426
Apoerythroprotein	221
Apomorphine hydrochloride, chemical data	103
- posology	370, 403
Apostilb	72
Apothecaries' measures	51, 55
Aqueous humour (eye)	362, 363
Aqueous solutions. See Solutions	
Arachidonic acid	223
Area units	53
Areca, Arecoline, posology	371
Areometer scales, conversion	109
Argentum. See Silver	
Arginase, in blood	324
L(+)-Arginine	224, 225
- in breast milk	228
- in plasma, free	317
- of plasma proteins	315
- in urine	289
Argon, properties and isotopes	86
Argon, ROBERTSON pupil	359, 360

A	page
Arithmetic mean	32
Arsenic, poisoning	422
- properties and isotopes	87
Arsenicals, international standards	79
- posology	371, 404
Arsenical solution, posology	371
Arsine poisoning	423
Arterial blood. See under Blood	
ARZNEIBUCH, DEUTSCHES, maximal doses	367 sq.
ASCHHEIM-ZONDEK test	179
Ascorbic acid. See Vitamin C	
- test, SAYERS'	182
L(-)-Asparagine	224
L(-)-Aspartic acid	224
- in plasma, free	317
- of plasma proteins	315
- in urine	289
Aspirin. See Acetylsalicylic acid	
Astatine, properties and isotopes	95
Astronomical data	81, 82
- unit (A.U.)	52
- units	52, 56, 82
- year	56
AT 10. See Dihydratichysterol	
Atebrin. See Mepacrine	
Atmosphere, composition	84 sq.
Atmosphere (unit), physical	61
- technical	60
Atomic constants	80, 81
Atomic weights, of elements and isotopes	82, 84 sq.
- of elementary particles	80
- of nuclei	80
Atomic numbers of elements	82, 84 sq.
ATP. See Adenosine triphosphate	
Atrium, right, blood pressure in	302
Atropine, chemical data	103
- poisoning	423
- posology	371, 404
- effect on pupil	357
A.U. (astronomical unit)	52
AUB and DUBOIS standard for B.M.R.	247
Auditory threshold	73
AUGSBERGER's dosage rule	401
Aureomycin. See Chlortetracyclin and Tetracyclins	
Aurum. See Gold	
Avidin	218
AVOGADRO's constant	75, 79
- number	55, 75, 79
Avoirdupois weight	55
Axerophthol. See Vitamin A	
Azolitmin, indicator range	106
Azoospermia	279

B

b (bar)	60
bbl. (barrel)	54
bu. (bushel)	54
B ₁ , vitamin	214
B ₂ , vitamin	215
B ₆ , vitamin	217
B ₁₂ , vitamin	221
Bacitracin	182
- international standard	79
Bacteria, and antibiotics	128 sq.
- classification	169 sq.
- pathogenic, index	172 sq.
BAL. See Dimercaprol	
BALLING hydrometer scale	109
Band cells, in blood and bone marrow	340
BANG's disease	141
Bar (pressure unit)	60
Barbital. See Barbitone	
Barbitone, chemical data	103
- and sodium derivative, posology	371, 404
Barbiturates, and gonadotropin secretion	180
- effect on pupil	357
- poisoning	423
Barium, compounds, chemical data	104
- poisoning	423
- properties and isotopes	90
Barometer corrections	127
Barometric units	60

B	page
Barrel (unit)	54
Basal metabolism (B.M.R.)	244 sq.
- age variation	24
- AUB and Du Bois standard	24
- BOOTHBY et al. standard	24
- nomogram for	24
- FLEISCH standard	24
- HARRIS-BENEDICT standard	24
- LEWIS et al. standard	24
- and menstrual cycle	24
- and pregnancy	24
- and protein-bound iodine	244, 32
- ROBERTSON and REID standard	24
- SHOCK standard	24
Base of natural logarithms (e)	7, 1
Bases, in blood	32
- in serum	32
- nomogram for	30
- excess, in foods	231 sq.
- in breast milk	22
BASEDOW's disease	20
Base-formers in blood	327, 32
Basophils (granulocytes)	33
- genealogy	33
- and growth	33
Basophilic erythrocytes	33
BAUMÉ hydrometer scales	10
Bc, vitamin	21
Bearded daniel, effect on pupil	33
BECK hydrometer scale	10
Belladonna (See also Atropine)	
- poisoning	42
- posology	372, 40
BENCE-JONES protein bodies, in urine	29
BENEDICT's test (urine)	29
Benzene, poisoning	42
- posology	37
Benzyl benzoate, posology	37
Benzyl orange, indicator range	10
Benzylpenicillin. See Penicillin G	
Beri-beri, and vitamin B ₁	2
Berkelium, properties and isotopes	1
BERNOULLI distribution	1
Beryllium, properties and isotopes	1
Beta rays of radio-isotopes	1
Beverages, chemical composition	242, 2
Bicarbonates (See also under Carbon dioxide)	
- conversion factors for carbon dioxide	120, 3
- in intestinal juice	2
- in pancreatic juice	2
- in serum	297, 3
Bicarbonate-CO ₂ . See Alkali reserve	
Bile, composition	2
- electrolytes	2
Bile acids, in blood	3
Bile pigments, in blood	319
- in faeces	2
Bile salts, in bile	2
- in blood	3
Bilharziasis	1
Bilirubin, in plasma	319, 3
- in urinary sediments	292, 2
- in urine	2
Binomial distribution	1
Biological standards, international	77
Biotin	218, 2
Birth. See under Pregnancy	
Bismuth, compounds, posology	3
- properties and isotopes	4
Bitter almonds and oil, poisoning	4
Bleeding time, capillary	3
Blind spot, demonstration	3
Blocking antibodies	341
Blood (See also Erythrocytes, Leucocytes, etc.)	
- acetoacetic acid	3
- acetone bodies	3
- acetylcholine	3
- ACTH	1
- adenosine triphosphate	3
- adrenaline and noradrenaline	3
- alcohol	3
- alkali reserve	297, 330,
- allantoin	297
- aluminium	297
- amino-acids, free	297
- anions	297
- bases	297

Note that this index does not include the Supplement (pages 427-519).

This has been separately indexed on pages 520-528.

Blood (continued)

Calcium

The following special indexes are also available:

Symbols and abbreviations for units page 50

Names and symbols of the elements page 83

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

B	page
Blood (<i>See also Erythrocytes, Leucocytes, etc.</i>)	
- bilirubin	319
- bleeding time, capillary	309
- bromine	329
- calcium	297, 327
- carbohydrates	320
- carbon dioxide	297, 330, 331
- carotenes, in disease	208, 209
- cations	297, 327
- cephalin	321
- chlorides	297, 326
- cholesterol	321
- choline	318
- circulation, effect of adrenaline and noradrenaline	205
- circulation time	301
- citric acid	322
- clot-retraction	310
- coagulation, theories	311, 312
- - time	309
- - and vitamin K	212
- coenzymes	324
- colloid-osmotic pressure	296, 305
- colour index	337
- copper	330
- cord, plasma proteins	273
- corpuscles. <i>See Erythrocytes, Leucocytes, etc.</i>	
- corticosteroids	182
- count	335, 339
- creatine, creatinine	318
- deoxyribonucleic acid	318
- electrical conductivity	308
- electrophoretic mobilities	309
- enzymes	324
- eosinophils	339
- ergothioneine	319
- erythroblasts	334
- erythrocytes (<i>See also under Erythrocytes</i>)	
- E.S.R.	306, 307
- ethyl alcohol	323
- fats	321
- fluorine	329
- formed elements	332 sq.
- freezing-point depression	116, 296, 305
- fumaric acid	322
- gallic acid and salts	321
- gases	330, 331
- glucosamine	320
- glucose	320
- glutathione	319
- glycogen	320
- groups	341 sq.
- - ABO	344
- - - sera for determining	77
- - and blood transfusion	343
- - Cellano	350
- - Duffy	351
- - Jay	351
- - Kell	350
- - Kidd	350
- - Lewis	350
- - Lutheran	350
- - MNSs	345
- - Pp	345
- - Rh	346
- - secretor/non-secretor	351
- guanidinoacetic acid	318
- haematocrit value	305, 335
- haemoglobin	337
- heparin tolerance test	309
- hexuronates	320
- histamine	319
- hormones. <i>See under Hormones</i>	
- hydrogen-ion concentration	297, 308, 330
- β -hydroxybutyric acid	322
- indican	318
- intermediary metabolic products	322
- iodine	329
- iron	330
- α -keto-acids	322
- keto-compounds	322
- lactic acid	322
- lead	329
- lecithin	321
- leucocytes	339, 340
- lipids	321
- magnesium	327

B	page
Blood (<i>See also Erythrocytes, Leucocytes, etc.</i>)	
- malic acid	322
- manganese	329
- methylguanidine	318
- nitrogen, distribution	317
- - free	330, 331
- - non-protein	317
- noradrenaline	205
- non-protein components	317, 318
- non-protein nitrogen	317
- nucleotides	318
- oncotic pressure	296, 305
- osmotic pressure	116, 296, 305
- osmotic resistance, erythrocyte	310
- oxygen	330, 331
- pentoses	320
- phenols	318
- phosphatase	325
- phosphates	297, 326
- phosphatides	321
- phospholipids	321
- phosphorus	297, 326
- plasma, composition of cerebrospinal fluid and	354
- plasma proteins	313 sq.
- - nomogram for	304
- - in pregnancy	272 sq.
- platelets. <i>See Thrombocytes</i>	
- polysaccharides	320
- potassium	297, 327
- in pregnancy	272 sq.
- preserved, electrolyte content	123
- pressure, diastolic and systolic	302
- - effect of adrenaline and noradrenaline	205, 206
- proteins	304, 313 sq.
- prothrombin time	310
- purine derivatives	318
- pyruvic acid	322
- "reducing substances"	320
- refractive index	307
- regeneration, and bilirubin	319
- reticulocytes	334
- ribonucleic acid	318
- sedimentation rate	306, 307
- serum proteins	297, 313
- serum water	298, 303
- silicon	327
- sodium	297, 327
- specific gravity	303
- specific heat	309
- sphingomyelin	321
- steroids	321
- succinic acid	322
- sulphates	326
- sulphur	326
- surface tension	307
- thrombocytes	338
- tin	329
- transfusion, and blood groups	343
- - and Rh blood groups	348
- typing sera, international standards	77
- uric acid	317
- uric acid	318
- viscosity	306
- vitamins	323
- volume, total	305
- zinc	330
Boas-Oppler bacillus	135, 286
Body, chemical composition	101, 282
Body fluids, distribution	295
- electrolytes	298
- osmotic relations	296
Body length, of adults	255
- of children	256 sq.
- of embryo	267
- of newborn and infants	256, 267
Body measurements, normal, during growth	256 sq.
Body surface area, of adults, Dubois formula and nomogram	250
- of adults and children, nomogram (leaflet inside back cover)	
- posology according to	401 sq.
Body weight, of adults	255
- of children	256 sq.
- distribution in organism	101, 282

B	page
Body weight, of embryo	267
- of newborn and infants	257, 267
- increase in pregnancy	272
Bohr's magneton	81
Bohr's radius of hydrogen atom	81
Boiling points of elements	84 sq.
Boltzmann's constant	81
Bone, chemical composition	282
Bone marrow, effect of ACTH/adrenocortical hormones	188
- myelogram	340
Borax, children's doses	405
Boric acid, chemical data	104
Bornhardt formula for body weight	255
Boron, properties and isotopes	84
Böttcher's crystals, in semen	278
Botulism	143
Brain, beef, chemical composition	240
Brain tumours and ocular symptoms	365, 366
Bread, chemical composition	236, 237
Breasts, physiology of	180
Breast milk. <i>See under Milk</i>	
BRITISH PHARMACEUTICAL CODEX, usual doses	367 sq.
BRITISH PHARMACOPOEIA, usual doses	367 sq.
British Thermal Unit	61
Brix hydrometer scale	109
Broca formula for body weight	255
Bromine, in whole blood	329
- chemical data	104
- poisoning	423
- properties and isotopes	87
Bromochlorophenol blue, indicator range	106
Bromocresol green, Bromocresol purple, indicator ranges	106
Bromoform, chemical data	103
- posology	373, 405
Bromophenol blue, Bromophenol red, indicator range	106
Bromothymol blue, indicator range	106
Bromvaletone, posology	373
<i>Brucella abortus</i>	141
- antiserum, international standard	77
Brucellosis	141
BTU (British Thermal Unit)	61
Buffer solutions	105
Buffering action of blood	297, 330
Butacaine sulphate, chemical data	103
Butazolidin. <i>See Phenylbutazone</i>	
BUTLER's infusion solutions	125
C	
c (carat)	55
c (centesimal minute)	57
c (curie)	70
cal (calorie)	61
cc (centesimal second)	57
cd (candela)	72
C (coulomb)	66
C, vitamin	213
CABOT's rings	334
Cadmium, properties and isotopes	89
Caecostomy secretion, electrolytes	298
Caeruloplasmin	314
Caesium, properties and isotopes	90
Caffeine, chemical data	103
- posology	373, 405
Calcibronat, children's doses	405
Calciferol (vitamin D ₂)	210
- children's doses	421
Calcium, acetate, electrolytic data	118-120
- in adrenals	282
- in blood	297, 327, 328
- in body and organs	282
- in bone	282
- in brain	282
- in breast milk	228
- chloride, chemical data	104
- - electrolytic data	118-120
- - solutions, specific gravity	109
- citrate, electrolytic data	118-120
- compounds, chemical data	104
- - posology	373, 405, 406
- in cow's milk	228

Note that this index does not include the Supplement (pages 427-519).

This has been separately indexed on pages 520-528.

Chorion

Calcium (continued)

The following special indexes are also available:

Symbols and abbreviations for units page 50

Names and symbols of the elements page 83

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

C	page
Calcium	
- in faeces	287
- in foods	231 sq.
- gluconate, blood circulation time measured by	301
- - electrolytic data	118-120
- - posology	373, 406
- glycerophosphate, chemical data	103
- in heart	282
- in intestinal juice	283
- in intestines	282
- ionized, in blood	327, 328
- in kidneys	282
- lactate, electrolytic data	118-120
- laevulinate, electrolytic data	118-120
- in lens (eye)	363
- in liver	282
- in lungs	282
- mandelate, chemical data	103
- in muscle	282
- oxalate, in urinary sediments	292, 293
- oxide, electrolytic data	118
- in pancreas	282
- in pancreatic juice	283
- phosphate, electrolytic data	118-120
- - in urinary sediments	292, 293
- properties and isotopes	86
- in prostate secretion	278
- requirement, daily	226
- in saliva	283
- salts, electrolytic data	118-120
- in semen	278
- in skin	282
- in spleen	282
- in testes	282
- thiosulphate, electrolytic data	118-120
- in urine	290
- in uterus	282
Calf circumference of children	260 sq.
Californium, properties and isotopes	97
Calorie	61
Calories, in breast milk	228
- in carbohydrates, fats and proteins	245
- consumption, and basal metabolism	244
- - and extrarenal water loss	296
- - standards	245 sq.
- - and vitamin B ₁	214
- in cow's milk	228
- daily requirements	226
- in foods	230 sq.
Cambogia, posology	373
Camera anterior	362
Camoquine. See Amodiaquine	
Camphor, chemical data	103
- posology	373, 406
Candela	72
Candida albicans	168
Cane sugar (<i>See also</i> Sucrose), chemical composition	238, 239
Cantharides, Cantharidin, posology	374
Capacity, electrical	66
- vital. <i>See</i> Vital capacity	
Capillary bleeding time	309
- blood pressure	296, 302
- permeability, and vitamin C	213
- - and vitamin P	214
- transudation	296
Capric, Caproic, Caprylic acids, in breast milk	229
Carat	55
Carbachol, posology	374, 406
Carbamino-carbon dioxide, in blood	331
Carbarsone, chemical data	103
- posology	374
Carbo adsorbens, children's doses	406
Carbohydrates (<i>See also</i> Glucose, Reducing substances, etc.)	
- in aqueous humour (eye)	363
- in blood	320
- calorific value	245
- in cerebrospinal fluid	353, 354
- in foods	230 sq.
- in lacrimal secretion	362
- in lens (eye)	363
- metabolism, and ACTH/adrenocortical hormones	187
- - and growth hormone	192
- - hormone of	181

C	page
Carbohydrates, metabolism	
- - index (CMI)	322
- - and insulin	206
- - and vitamin B ₁	214, 322
- in plasma protein fractions	314
- in prostate secretion	278
- in semen	277
- in urine	289
- in vitreous humour (eye)	364
- water of oxidation	295
Carbolic acid. <i>See</i> Phenol	
Carbomycin	128 sq.
Carbon, properties and isotopes	84
- tetrachloride, poisoning	424
- - posology	374
- monoxide, in blood	338
- - poisoning	423
Carbon dioxide (<i>See also</i> Alkali reserve, Bicarbonates)	
- in aqueous humour (eye)	363
- in blood	330, 331
- - combined	331
- - "free"	331
- capacity, of blood	330, 331
- carbamino-, of blood	331
- chemical data	104
- combining capacity,	330
- - of blood	297, 331
- - of spinal fluid	353
- conversion factors for bicarbonate and pH of blood	120, 330
- liberation for proteins, fats and carbohydrates	245
- in prostate secretion	278
- in semen	278
Carbonic acid, in blood	330
Carboxyhaemoglobin	338
Carbromal, chemical data	103
- posology	374, 406
Carcinoma, gastric, and gastric juice	286
Cardiolipin, international standard	78
Carlsbad salt, children's doses	406
Carotenes (<i>See also</i> Vitamin A)	209, 210
- and thyroid function	210
β-Carotene, international standard	78
CARTIER hydrometer scale	109
Casein, amino-acid composition	229
- in breast milk	228
Cassiopeium, properties and isotopes	92
Casts, urinary	292
Castor oil, posology	374, 406
Catalase, in plasma	325
Catechin, vitamin-P activity	214
Cations, in blood	297, 327
- definition	115
- in various electrolytes	118-120
- in urine	290, 299
Cat-scratch disease	157
Caustic potash, Caustic soda, poisoning	422
Cell count. <i>See</i> Blood count	
Cellano blood group	350
Celsius. <i>See</i> Centigrade	
Centigrade temperature scale	56
- conversion to Fahrenheit scale	58
Centimetre	52
Centimetre ⁻¹ (energy unit)	61
Centimetre-milligram-element hour	71
Cephalin, in plasma	321
Cereal products, chemical composition	236, 237
Cerebellar tumours, ocular symptoms	366
Cerebellopontile angle, tumours, and ocular symptoms	366
Cerebrospinal fluid	352 sq.
Cerebrospinal meningitis	132, 137
Cerium, properties and isotopes	90
Cervix uteri, pH value	276
CGS system of measurement	49 sq.
Chamber, anterior, of eye	362
CHARCOT-NEUMANN crystals, in semen	278
CHAUVENET's criterion	47
Chemical composition, of blood	313 sq.
- of body	101, 282
- of breast milk	228, 229
- of foods	230 sq.
- of gastric juice	284 sq.
- of milk	228, 229
- of organs	282

C	page
Chemical composition	
- of urine	288 sq.
Chemical scale of atomic weights	80
Chemical units	75, 76
Chenopodium, poisoning	424
- posology	374, 406
Chest circumference during growth	257 sq.
Chiasma, glioma of, ocular symptoms	366
Chiasmal syndrome	365
Children (<i>See also</i> Growth, Infants, Newborn)	
- basal metabolism	246 sq.
- formed elements in blood	333, 339
- normal body measurements	256 sq.
- posology	401 sq.
- skeletal development	268 sq.
- vital capacity	252-254
Chiniofon sodium, posology	375, 407
Chloral hydrate, chemical data	103
- poisoning	424
- posology	375, 407
Chloramphenicol, chemical data	103
- international standard	79
- and pathogenic agents	129 sq.
- posology	375, 407
Chlorbutol, posology	375
Chlorguanide. <i>See</i> Proguanil	
Chlorides. <i>See</i> under Chlorine	
Chloride shift, in blood	326
Chlorine, in aqueous humour of eye	363
- in bile	298
- in blood	297, 326
- in body and organs	282
- in breast milk	228
- in caecostomy secretion	298
- chemical data	104
- in cow's milk	228
- in faeces	298
- in foods	231 sq.
- in gastric juice	284 sq., 298
- in ileal secretion	298
- in intestinal juice	298
- in lacrimatory secretion	362
- in lens of eye	363
- in pancreatic juice	298
- poisoning	424
- properties and isotopes	85
- in prostate secretion	278
- in saliva	298
- in semen	278
- in serum ultrafiltrate, serum water	298
- in sweat	298
- in transudates	298
- in urine	299
Chloroform, chemical data	103
- poisoning	424
- posology	375
Chloromycetin. <i>See</i> Chloramphenicol	
Chlorophenol red, indicator range	106
Chloroquine, chemical data	103, 161
- in malaria	161
- posology	161, 375
Chlortetracyclin, international standard	79
- and pathogenic agents	129 sq.
- posology	375, 404
Cholera	129, 130
- agglutinating sera, international standards	77
- antigens and vaccines, international standards	78
Cholesterol, in bile	283
- in blood	321
- in cerebrospinal fluid	353
- chemical data	103
- esters, in blood	321
- in plasma proteins	314
- in prostate	278
- and protein-bound iodine	329
- in semen	277
- structural formula	195
- in urinary sediments	292, 293
Cholic acid, in serum	321
Choline	222
- in blood	318
Cholinergics, poisoning	422
- effect on pupil	357
Cholinesterase, in blood	325
- in plasma proteins	314
Chorion, diameter	267

Note that this index does not include the Supplement (pages 427-519).

This has been separately indexed on pages 520-528.

Diabetes mellitus

Symbols and abbreviations for units page 50

Names and symbols of the elements page 83

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

The following special indexes are also available:

C page

Chorionic gonadotropins 179
 Choroid 357
 Chromatic scale 74
 Chromic acid poisoning 424
 Chromium, poisoning 424
 - properties and isotopes 86
 Chyluria 289
 Cibalgin, children's doses 407
 Ciliary body and muscle 357
 Cinchophen, chemical data 103
 Circulation, blood. See under Blood
 Cisternal fluid, sugar content 354
 (See also under Cerebrospinal fluid)
 Cis-trans isomerism of steroids 195
 Citric acid, in aqueous humour (eye) 363
 - in blood 322
 - chemical data 104
 - in foods 231 sq.
 - in prostate secretion 278
 - in semen 277
 - in urine 289
 Citrin (vitamin P) 214
 Citrovorum factor 219 sq.
 Citrulline 224
 - in plasma 317
 Cl (clausius) 62
 CLARK'S rule 401
 CLARK and LUBS' buffer solutions 105
 Clausius (entropy unit) 62
 Clivus border syndrome 365
 Clostridium welchii antitoxins, standard 77
 Clot retraction time 310
 Clotting time 309
 Clupanodonic acid 223
 Coagulation theories, blood 311, 312
 Coagulation time, blood 309
 - semen 276
 Cobalamine. See Vitamin B₁₂
 Cobalt, properties and isotopes 87
 Coca, posology 375
 Cocaine, chemical data 103
 - poisoning 424
 - posology 375
 - effect on pupil 357
 Cocarboxylase 214
 - in erythrocytes 324
 Codehydrases I and II 218
 Codeine, chemical data 103
 - poisoning 425
 - and salts, posology 375, 376, 407
 CODEX GALLICUS, usual doses 367 sq.
 Cod-liver oil, posology 376, 407
 Coeliaca, and folic acid 220
 Coenzymes, in blood 324
 - I and II 218
 Coenzyme A 216
 - in blood 324
 - in erythrocytes 324
 Co-ferments. See Coenzymes
 Colchicine, chemical data 103
 - posology 376
 COLLIP unit for parathyroid hormone 207
 Colloid-osmotic pressure of serum 296, 305
 Colocynth, posology 377
 Colostrum, chemical composition 228, 229
 Colour blindness, test charts (inside back cover)
 Colour index of blood 337
 Colour vision, fields 361
 Columbium. See Niobium
 Compounds A, B, E, F 196
 COMPTON'S wave-length of electron 81
 Concentration, capacity of kidneys 299, 300
 - test for renal function 299, 300
 - units 76, 114, 115
 Conductivity, electrical. See Electrical
 conductivity
 - thermal, units 63
 Cones, retinal 359
 Confectionery, chemical composition 238, 239
 Congo red, indicator range 106
 Connective tissue, effect of ACTH and
 adrenocortical hormones 188
 Consonance and dissonance 74
 Constants, astronomical 56, 81, 82
 - atomic 80, 81
 - cosmic 81, 82
 - mathematical 7

C page

Constants
 - of elementary particles 80
 - physical 79, 80
 Contra-insular principle of pituitary 181
 Convergence reaction, pupillary 358
 - and headache 364
 Conversions, of equivalents, grams, moles,
 osmoles 115
 - of temperature scales 58
 Conversion factors, for bicarbonate and
 carbon dioxide 120, 330
 - for particular electrolytes 118-120
 - for serum electrolytes 297
 - stoichiometric, for medically important
 compounds 126
 - for units. See under Units
 COOMBS test 341, 343
 Copper, in breast milk 228
 - in cow's milk 228
 - in foods 231 sq.
 - in lens (eye) 363
 - in organs 282
 - oxide, chemical data 104
 - in plasma 330
 - properties and isotopes 87
 - daily requirement 227
 - sulphate, chemical data 104
 - posology 377
 Coproporphyrins, in blood 338
 - in urine 291
 Coramine. See Nikethamide
 Cornea 356
 - and ophthalmological headache 364
 Corpus ciliare 357
 Corpus vitreum 364
 Corpuscular radiation units 71
 Correlation, statistical 42 sq.
 Corrosive sublimate. See Mercuric chloride
 Cortex, adrenal. See Adrenal cortex
 Cortexone 203
 - chemistry 196
 - function, etc. 182 sq.
 - metabolism 199
 Cortical hormones. See Corticosteroids
 Corticosteroids 203
 - chemistry 196
 - function, etc. 182 sq.
 - insufficiency 189
 - metabolism 197-199
 - overdoses, physiological effects 186
 Corticosterone 203
 - chemistry 196
 - function, etc. 182 sq.
 - metabolism 197
 Corticotropin. See ACTH
 Cortisol. See Hydrocortisone
 Cortisone 203
 - acetate, children's doses 408
 - chemistry 196
 - function, etc. 182 sq.
 - metabolism 197
 Cosmic constants 81, 82
 Cotarnine chloride, posology 377
 Coulomb 66
 Coumarin, chemical data 103
 Cover test for strabismus 365
 Cow manure factor. See Vitamin B₁₂
 Coxsackie virus 154
 Cozymase 218
 Craniopharyngioma, and ocular symptoms 366
 Creatine, Creatinine, in breast milk 228
 - in cerebrospinal fluid 353
 - chemical data 103
 - clearance, and renal function 300
 - nitrogen, conversion factors 126
 - in plasma 318
 - in urine 288
 Creosote, posology 377
 Cresols, chemical data 103
 m-Cresol purple, indicator range 106
 Cresol red, indicator range 106
 o-Cresolphthalein, indicator range 106
 Cross-matching (blood) 343
 Croton oil, posology 377
 Cryptagglutinoids 341 sq.
 Cryptoxanthin 209
 Crystal violet, posology 377, 408

C page

α- and β-Crystallins, in lens of eye 363
 C.S.F. See Cerebrospinal fluid
 Cubic measures 53
 Curie 70
 CURIE constant 81
 Curium, properties and isotopes 97
 Current density and strength, electrical 65
 CUSHING'S syndrome 183, 193
 CV (horse-power) 62
 Cyanide poisoning. See Prussic acid 426
 Cyanocobalamin. See Vitamin B₁₂
 Cycle, menstrual. See Menstrual cycle
 Cyclobarbitone, and calcium salt, posology 377
 Cyclopropane, chemical data 103
 Cylinders, urinary 292
 L(-)-Cysteine 224, 225
 - in plasma 317
 - of plasma proteins 315
 - in urine 289
 - in urinary sediments 292, 293
 L(-)-Cystine 224
 - in plasma 317
 - of plasma proteins 315
 - in urine 289
 - in urinary sediments 292, 293
 Cystinuria 290
 Cytochrome C reductase 216

D
 db (decibel) 73
 dwt. (pennyweight) 55
 dyn (dyne) 59, 69
 D, D₂, D₃, D₄, D₅, vitamins 210

 DAB. See DEUTSCHES ARZNEIBUCH
 Dairy products, chemical composition 238 sq.
 Dalton (mass unit) 55
 Dark adaptation of eye 358
 - and photometric units 72
 DARROW'S infusion solutions 125
 DAVIDSEN and KJERULF-JENSEN infusion
 solutions 125
 Decenoic acid, in breast milk 229
 Decibel 73
 Decholin, measurement of circulation time by 301
 Deficiency anaemia 220-222
 Degree (angle) 57
 - (temperature) 56, 57
 Dehydrases 216
 Dehydroepiandrosterone, activity 201
 - chemistry 196
 - metabolism 198
 Dehydroisoandrosterone. See Dehydroepi-
 androsterone
 Dehydroascorbic acid 213
 7-Dehydrocholesterol, vitamin D₃ from 210
 Dehydrocholic acid. See Decholin
 Dehydrocorticosterone 203
 - chemistry 196
 - metabolism 197
 7-Dehydrositosterol, vitamin D₅ from 210
 Density, definition and units 60
 - of the elements 84 sq.
 - hydrometer scales for 109
 (See also Specific gravity)
 Deoxy-. See Desoxy-
 Desoxycorticosterone. See Cortexone
 Desoxycortone acetate, posology 377
 Detoxication, and glucuronic acid 289
 - and inorganic sulphur 290
 Deuteranomalopia, Deuteranopia
 (test charts inside back cover)
 Deuterium, atomic constants 80
 Deuterons, biological activity 71
 - constants 80
 DEUTSCHES ARZNEIBUCH, maximal doses 367 sq.
 Dextrose. See Glucose
 DFP. See Diisopropyl fluorophosphate
 Diabetes mellitus, and acetone bodies in urine 289
 - and acidosis 297
 - and ACTH 187, 193
 - and adrenocortical hormones 187, 192 sq.
 - and blood sugar 320
 - and gonadotropic hormones 180
 - and growth hormone 192 sq.

Note that this index does not include the Supplement (pages 427-519).
This has been separately indexed on pages 520-528.

Erythrocyt

Diabetes mellitus (continued)

The following special indexes are also available:

Symbols and abbreviations for units page 50

Names and symbols of the elements page 83

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

D	page
Diabetes mellitus, and insulin.	206
Diabetogenic action, of ACTH and cortico-steroids	187
- of growth hormone	192
Diaphorases	216
Diarrhoea. See under Dysentery and Enteritis	
Diastase. See Amylase	
Diastolic pressure. See under Blood pressure	
Diatonic scales	74
Dicoumarol, and derivatives, and vitamin K ₁	213
- posology	377
Dielectric constant of vacuum	64, 65
- polarization	66
Dienoestrol, posology	377
Diethylbarbituric acid. See Barbitone	
Diethylene glycol, poisoning	424
Diethylstilboestrol. See Stilboestrol	
Digitalis, international standard	79
- poisoning	424
- posology	377, 378, 408, 409
Digitonin, Digitoxin, chemical data	103
Dihydrocodeine bitartrate, children's doses	409
Dihydrocodeinone bitartrate, posology	378, 409
22-Dihydroergosterol, vitamin D ₄ from	210
Dihydrohydroxycodone, posology	378
Dihydromorphinone, chemical data	103
- posology	378
Dihydrostreptomycin, chemical data	103
- international standard	79
- toxicity	128
- posology	378
Dihydrotachysterol, in hypoparathyroidism	211
Dihydrotestosterone	196
Di-iodohydroxyquinoline, chemical data	103
Di-iodotyrosine	208
- posology	378
Dilution test for renal function	288
Dimensions, physical, definition	49
Dimercaprol (BAL), in arsenic poisoning	422
- chemical data	103
- and enzyme blocking	215
- international standard	79
- in mercury poisoning	425
- posology	378
2:3-Dimercaptopropanol. See Dimercaprol	
Dimethylaminoantipyrine. See Amidopyrine	
<i>p</i> -Dimethylaminoazobenzene, indicator range	106
<i>m</i> -Dinitrobenzene, chemical data	103
Dinitrophenols, indicator ranges	106
Dioxan, chemical data	103
- poisoning	424
Diphenylhydantoin. See Phenytoin	
Diphosphoglycerates, in blood	326
Diphosphoinositide	223
Diphosphopyridine nucleotide	218
- in blood	324
Diphtheria, and antibiotics	135
- antitoxins, international standards	77
- SCHICK-test toxin, international standard	78
- toxoid, international standard	78
Diseases, infectious. See Infectious diseases	
Disintegration, radioactive. See Radioactive disintegration	
Dispersion constant	81
Dissonance and consonance	74
Distributions, statistical	30 sq.
<i>t</i> -Distribution	30, 38
χ^2 -Distribution	30, 39
Diuresis	288
- electrolyte retention in	299
- in isosthenuria	299
Dodecenoic acid, in breast milk	229
Doses. See Posology	
Dose constant, radiation	71
DOVER's powder, posology	383, 410
DPN. See Diphosphopyridine nucleotide	
Drachm, Dram	54, 55
Drugs, and colour of faeces	287
- and colour of urine	291
- posology, adult	367 sq.
- in childhood	401 sq.
Du Bois formula for body surface	250
Duffy blood group	351
DUKE method for capillary bleeding time	309
Duodenum, pH value	283
Dwarfism, pituitary	193
Dyne	59, 69

D	page
Dysentery, amoebic	157
- antiserum, international standard	77
- bacillary	139, 140
Dysprosium, properties and isotopes	91

E	page
<i>e</i> (base of natural logarithms)	7, 17
emu (electromagnetic unit)	64
equ., equiv. (equivalent)	75, 114, 297
esu (electrostatic unit)	64
eV (electron volt)	61
E, vitamin	211

Earth, constants	81
Earth's crust, abundance of elements	84 sq.
Eelworm	168
Eggs, chemical composition	238, 239
Eicosatetraenoic acid, in breast milk	229
Einsteinium	97
Ejaculate. See under Semen	
Electric charge, of electron	80
- of erythrocytes	309
- units	66
Electrical conductivity	67
- of aqueous humour (eye)	362
- of blood serum	308
- of cerebrospinal fluid	352
- of semen	277
- of vitreous humour (eye)	364
Electrical potential	64
Electrical resistance	66
Electrical units	64 sq.
Electrolytes (See also Solutions) 114-120, 295-300	
- in aqueous humour (eye)	363
- in bile	298
- in blood	297, 326 sq.
- in caecostomy secretion	298
- in cerebrospinal fluid	353, 354
- conversion tables	118-120
- definition	115
- in faeces	298
- in gastro-intestinal secretions	284, 298
- in ileal secretion	298
- in infusion solutions	124, 125
- in lacrimal secretion	362
- in lens (eye)	363
- metabolism, and ACTH/adrenocortical hormones	187
- and posterior pituitary hormones	194
- in pancreatic juice	298
- for parenteral infusion	121 sq.
- in prostate secretion	278
- replacement, infusion solutions for	121 sq.
- in saliva	298
- in semen	277
- in serum	297
- in serum ultrafiltrate, serum water	298
- in sweat	298
- in transudates	298
- in urine	299

Electrolytic solutions. See Electrolytes and Solutions	
Electromagnetic CGS-system	64 sq.
Electron, constants	80, 81
Electron-volt	61
Electrophoretic mobility of erythrocytes and plasma proteins	309
- protein fractions, cerebrospinal fluid	352
- plasma	313
Electrostatic CGS-system	64 sq.
Elements, alphabetical tables	83
- periodic system	82
- properties and isotopes	84 sq.
Elementary charge, length, time	80
Elephantiasis	165
ELKINGTON and TARAIL's infusion solutions	125
Elliptocytes, Elliptocytosis	336
Emanation, radium. See Radon	
Embryo, size and weight	267
Emetine hydrochloride, chemical data	103
- posology	379, 409
Energy, mass equivalents	80
- units	61, 69
Enteritis	137-139

E	page
Enzymes (See also Coenzymes)	
- in blood	324, 3
- gastric	284, 2
- intestinal	2
- lab	2
- oxidation	215, 2
- respiratory	215, 2
- SCHARDINGER's	2
- WARBURG's respiratory	215, 2
- yellow	215, 2
Eosinopenia. See under Eosinophils	
Eosinophils (granulocytes)	3
- and ACTH/adrenocortical hormones	1
- and adrenaline	189, 2
Ephedrine, chemical data	1
- effect on pupil	3
- posology	379, 4
Epiandrosterone. See epiAndrosterone	
Epicatechin, vitamin-P activity	2
Epididymis, and semen volume	2
Epinephrine. See Adrenaline	
Epiphysal tumours, ocular symptoms	3
Epsom salts. See Magnesium sulphate	
Equilenin, Equilin	1
Equivalent, chemical	75, 114, 2
Erbium, properties and isotopes	61,
Erg	61,
Ergometrine (ergonovine), chemical data	1
- posology	3
Ergosterol, vitamin D ₂ from	2
Ergot, posology	3
Ergotamine, chemical data	1
- effect on pupil	3
- posology	3
Ergothioneine, in blood	3
Ergotoxin, effect on pupil	3
Eriodictyol, vitamin-P activity	2
Erosio interdigitalis	1
Errata and addenda	1
Errors, distribution of. See Normal distribution	
Erysipelas, swine	1
- international standard serum	1
Erysipeloid	1
Erythema dose, skin	3
Erythroblasts, in blood	3
- in bone marrow	3
Erythroblastosis foetalis	347, 3
Erythrocytes	334
- agglutination	341
- basophilic granulated	3
- carbon dioxide in	3
- carboxyhaemoglobin in	3
- chloride shift to	3
- cocarboxylase in	3
- coenzyme A in	3
- coproporphyrin in	3
- count (RBC)	3
- diameter	3
- electric charge	3
- electrophoretic mobility	3
- flavine adenine dinucleotide in	3
- genealogy	3
- glyoxalase in	3
- and growth	3
- pH value	3
- haemoglobin in	3
- inclusion bodies in	3
- lead in	3
- lifetime of	3
- methaemoglobin in	3
- nitrogen in	3
- non-protein nitrogen in	3
- numerical eccentricity of	3
- osmotic resistance of	3
- oxygen in	3
- packed cell volume. See Haematocrit value	
- phosphorus in	3
- polychromatic	3
- potassium in	3
- protoporphyrin in	3
- pyridine nucleotides in	3
- reticulated. See Reticulocytes	
- sedimentation rate	306, 3
- sodium in	3
- specific gravity of	3
- specific heat of	3
- surface area	3

Note that this index does not include the Supplement (pages 427-519).

This has been separately indexed on pages 520-528.

Globulins

Erythrocytes (continued)

The following special indexes are also available:

Symbols and abbreviations for units page 50

Names and symbols of the elements page 83

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

E	page
Erythrocytes, thickness	336
- verdohaemoglobin in	338
- volume of, total	305
- mean corpuscular volume	335
- zinc in	330
Erythromycin	128 sq.
Erythroprotein, and vitamin B ₁₂	221
Eserine. See Physostigmine	
Esophoria	364, 365
E.S.R. (erythrocyte sedimentation rate)	306, 307
Essential amino-acids	225
- fatty acids. See Vitamin F	
- hypertension	302
- oils, poisoning. See Volatile oils	426
Estrogens. See Oestrogens	
Ether, chemical data	103
- blood circulation time measured by	301
Ethereal oils, poisoning. See Volatile oils	426
Ethinylloestradiol, posology	379
Ethisterone, posology	379
Ethyl alcohol, in blood	323
- chemical data	103
- and coproporphyrin excretion	291
- poisoning	323, 422
- effect on pupil	357
- solutions, specific gravity	111
Ethyl biscoumacetate, posology	379
Ethylene glycol, poisoning	424
Ethyl ether. See Ether	
Ethylhydrocupreine, posology	379
Ethylmorphine, chemical data	103
- posology	379
N-Ethylpiperidine, chemical data	103
Etiane. See Aetiane	
Eucalyptol, chemical data	103
- poisoning	426
Eucatropine, chemical data	103
- effect on pupil	357
Euglobulin	313, 314
Europium, properties and isotopes	91
Evaporation, body water loss through	296
EWALD test meal	284
- gastric juice volume after	284
Exchange transfusion	348
Exophoria	364, 365
Exponential functions, tables	17 sq.
Extracellular fluid	295
Extrinsic factor, CASTLE'S. See Vitamin B ₁₂	
Eye	355 sq.
- aqueous humour	362
- ball	356
- blind spot	359
- choroid	357
- ciliary body	357
- cornea	356
- intraocular pressure	362
- iris	357
- lens	363
- muscles	355
- pupil	357
- retina	359
- sclera	356
- relative spectral sensitivity	72
- symptoms due to brain tumours	365, 366
- test charts	(inside back cover)
- visual fields	361
- visual pathway	360
- vitreous humour	364
Eyeball	356
Eye worm, African	166

F	page
F (farad)	66
F, vitamin	223

Factorials 1-100	24
Faeces	287
- electrolytes	298
Fahrenheit temperature scale	57
- conversion to Centigrade scale	58
Farad	66
Faraday, definition	75
FARADAY'S constant	80
Farsightedness	364
Fats, in blood	321

F	page
Fats, in body and organs	282
- in breast milk	228, 229
- calorific value	245
- in cow's milk	228
- edible, chemical composition	238, 239
- in faeces	287
- in foods	230 sq.
- in lens (eye)	363
- metabolism, effect of ACTH/adrenocortical hormones	187
- neutral, conversion factors for carbon	126
- in organs	282
- oxidation water of	295
- requirement, daily	227
- in urine	289
Fat-soluble vitamins	209 sq.
Fatty acids, in bile	283
- in blood	321
- in breast milk	229
- in faeces	287
- unsaturated (vitamin F)	223
- in urine	289
Feces. See Faeces	
FEHLING'S test (urine)	294
Ferments. See Enzymes	
Fermium	97
Ferric chloride solutions, specific gravity	108
Ferrihaemoglobin	338
Fertility, and spermatozoa	279, 280
Fertility index of spermatozoa, nomogram for	280
Fetus. See Embryo	
Fevers. See Index of diseases	172 sq.
Fibre content of foods	230 sq.
Fibrinogen	313 sq.
- amino-acid composition	315
- electrophoretic mobility	309
- and oncotic pressure	305
- and plasma viscosity	306
- in pregnancy	273
Fibroplesia, retrolental	31
(See also Addenda, page 4)	
Field strength, electric	65
- magnetic	67
Filariasis	165
Filicin extract. See Male fern extract	
Fine-structure constant, SOMMERFELD'S	81
Fish, chemical composition	242, 243
Flatworms. See Platyhelminthes	
Flavanols, Flavanones, Flavones, vitamin-P activity	214
Flour, chemical composition	236, 237
Fluid and electrolyte balance	295 sq.
Fluorescein, blood circulation time from	301
Fluorine, in blood	329
- poisoning	424
- properties and isotopes	85
Flux, magnetic	69
Foetus. See Embryo	
Folic acid	219, 220
- conjugase	325
- posology	380
Follicle-stimulating hormone (FSH)	179
Foods, chemical composition	230 sq.
- choline content	222
- inositol content	223
- protein amino-acids of	225
- stomach-emptying time for	286
- vitamin-B ₁₂ content	221
Food poisoning. See Botulism	423
Foot, secondary ossification centres	268, 270
Force units	59
Formaldehyde, chemical data	103
- poisoning	424
Formaldehydogenic steroids. See under Steroids	
Formalin. See Formaldehyde	
Formed elements in blood	332 sq.
Formulae of medically important compounds	103
5-Formyl-5:6:7:8-tetrahydropteroylglutamic acid. See Citrovorum factor	
FOSTER KENNEDY syndrome	365, 366
Fovea centralis, diameter	359
FOWLER'S solution, poisoning	422
- posology	371
FPS-system of measurement	49
Frankium, properties and isotopes	95
Freezing-point depression, of aqueous humour (eye)	362

F	page
Freezing-point depression	
- of bile	283
- calculation	115 sq.
- of cerebrospinal fluid	352
- of gastric juice	284
- of intestinal juice	283
- of lacrimal secretion	362
- of lens (eye)	363
- of pancreatic juice	283
- of saliva	283
- of serum	296, 305
- of urine	288
Frequency in chromatic scale	74
Frequency units	59
FRIEDMAN test for gonadotropins	179
Frog tests for gonadotropins	179
Frontal lobe tumours, and ocular symptoms	365
Fructose, and diabetes	206, 207
- in semen	277
- solutions, calculation of	117
- - calorific value	117
- in urine	289
Fruit, chemical composition	230 sq.
FSH (follicle stimulating hormone)	179
Fumaric acid, in blood	322
Fy antigens (blood group Duffy)	351

G	page
γ (gamma, microgram, μg)	55
g (gram)	55
gr. (grain)	55
g.atom (gram atom)	75, 114
g.equiv (gram equivalent)	75, 114, 297
G (gauss)	67

Gadolinium, properties and isotopes	91
Gal (galileo)	59
Galactic system, constants	82
Galactopoiesis	180
Galileo	59
Gallbladder, bile from	283
Gallium, properties and isotopes	87
GAMBLE'S ionogram	296, 297
Gamma (microgram)	55
Gamma rays, biological activity	71
- of radio-isotopes	100
- units	70, 71
Gas, domestic, poisoning. See under Carbon monoxide	423
Gas constant, universal	79
Gas gangrene. See Index of diseases	175
- antitoxins, international standards	77
Gases, in blood	330, 331
- ideal, molar volume	79
- volume, correction	127
Gasoline poisoning. See Petroleum spirit	425
Gastric carcinoma, and gastric juice	286
Gastric juice	284 sq.
- electrolytes	298
Gastric ulcers. See under Ulcers	
Gastritis, gastric juice in	286
Gastro-intestinal tract (See also Intestines, Stomach, etc.)	283 sq.
- and ACTH	188
- secretions, infusion solutions for replacing	123 sq.
- water loss via	296
Gauss (unit)	67
GAUSS distribution. See Normal distribution	
Gb (gilbert)	67
Genotypes (blood groups)	344 sq.
Gentian violet. See Crystal violet	
GERHARDT'S test (urine)	294
Germanium, properties and isotopes	87
GFR (glomerular filtration rate)	300
GH (growth hormone)	192, 193
Gigantism, pituitary	193
Gilbert	67
GIRARD'S reagent, chemical data	103
Glandotropic hormones	179 sq.
GLAUBER'S salt. See Sodium sulphate	
Glaucoma, ocular symptoms	364
Glioma of optic chiasma, and ocular symptoms	366
Globulins, of cerebrospinal fluid	352, 353

Note that this index does not include the Supplement (pages 427-519).

This has been separately indexed on pages 520-528.

Hydnocarpus oil

Globulins (continued)

The following special indexes are also available:

Symbols and abbreviations for units page 50

Names and symbols of the elements page 83

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

- | | | | | | |
|----------------------------------------------------|--------------|---------------------------------------------------------|---------------|------------------------------------------------------|----------|
| G | page | G | page | H | page |
| Globulins, of lacrimal secretion | 362 | Growth, blood in | 308 | Helium, atomic constants | 80 |
| - of pancreatic juice | 283 | - pH value | 308 | - properties and isotopes | 84 |
| - plasma | 313 sq. | - haematocrit | 335 | Helvellic acid, poisoning. See under | |
| - electrophoretic mobility | 309 | - haemoglobin | 337 | Mushrooms | 425 |
| - and plasma viscosity | 306 | - formed elements | 333 | Hemeralopia and vitamin A | 209 |
| - in pregnancy | 273 | - iodine | 329 | Hemo-. See Haemo- | |
| - serum | 313 sq. | - lactic acid | 322 | Hemianopia, and lesions of visual path | 360, 361 |
| - and oncotic pressure | 296, 305 | - leucocytes | 339 | - and brain tumours | 365, 366 |
| Globulinuria | 288 | - inorganic phosphorus | 326 | HENDERSON and HENDERSON-HASSELBALCH | |
| Glomerular filtration | 300 | - polysaccharides | 320 | equations | 297, 330 |
| Glomerular nephritis, and hypertension | 302 | - body measurements in | 256 sq. | Henry (unit) | 69 |
| Glucocorticosteroids | 203 | - body water in | 282, 295 | Heparin, international standard | 78 |
| Gluconeogenesis, and ACTH/adrenocortical | | - gastric secretion and proteases in | 284, 285 | - posology | 381 |
| hormones | 187 | - growth hormone and | 192, 193 | - tolerance tests | 309 |
| - and growth hormone | 192 | - 17-ketosteroids in | 183, 200, 201 | Hepatic duct, bile from | 283 |
| - and insulin | 206 | - oestrogens in | 201 | Hepatitis virus | 156, 157 |
| Glucosamine, in plasma | 320 | - ossification centres in | 268 sq. | <i>n</i> -Heptylpenicillin sodium, international | |
| Glucose, in aqueous humour (eye) | 363 | - posology during | 401 sq. | standard | 79 |
| - in blood | 320 | - pupillary diameter and | 357 | Heroin, poisoning. See Morphine | 425 |
| - in cerebrospinal fluid | 353 | - development of teeth in | 271 | Herpes simplex | 153 |
| - children's doses | 408 | - urine in | 288 | Hertz (unit) | 59 |
| - in lacrimal secretion | 362 | - vital capacity in | 254 | Hesperidin, Hesperitin, vitamin-P activity | 214 |
| - in lens (eye) | 363 | Growth hormone | 192, 193 | Heteroagglutinins | 341 |
| - solutions, calculation | 117 | Guaiacol, posology | 381, 409 | Heterophoria | 364, 365 |
| - calorific value | 117 | Guanidine, of plasma proteins | 315 | Hexadecenoic acid, in breast milk | 229 |
| - isotonic | 124 | Guanidinoacetic acid, in plasma | 318 | Hexamine, children's doses | 409 |
| - in urine | 289 | | | Hexeton, children's doses | 409 |
| - in vitreous humour (eye) | 364 | H | | Hexobarbitone, and sodium salt, posology | 381 |
| Glucosides. See Glycosides | | <i>b</i> (PLANCK's constant) | 62, 80 | Hexosamine, in aqueous humour (eye) | 363 |
| Glucuronic acid, in urine | 289 | h.p. (horse-power) | 62 | Hexose phosphate, in blood | 326 |
| Glucuronidase, in blood | 325 | H (henry) | 69 | Hexuronates, in blood | 320 |
| L(+)-Glutamic acid | 224, 225 | | | Hexylresorcinol, children's doses | 410 |
| - in plasma | 317 | Haematocrit value, and blood specific gravity | | Hippuric acid, in urinary sediments | 292, 293 |
| - of plasma proteins | 315 | (nomogram) | 304 | - in urine | 288 |
| - in urine | 289 | - and blood viscosity | 306 | Histaminase, in blood | 325 |
| L(+)-Glutamine | 224 | - variation during growth | 333 | Histamine, chemical data | 103 |
| Glutathione, in whole blood | 319, 320 | - total | 305 | - in plasma | 319 |
| Glycerol, chemical data | 103 | - venous | 335 | - posology | 381 |
| Glyceryl trinitrate, posology | 380 | - and water balance | 295 | - effect on pupil | 357 |
| Glycine | 224, 225 | Haematoidin, in urinary sediments | 292 | L(-)-Histidine | 224, 225 |
| - in plasma | 317 | Haematopoiesis, and ACTH/adrenocortical | | - in breast milk | 228 |
| - of plasma proteins | 315 | hormones | 188 | - in plasma | 317 |
| Glycocholates, in bile | 283 | - and blood porphyrins | 338 | - of plasma proteins | 315 |
| Glycocholic acid, in blood | 321 | - and folic acid group | 220 | - in urine | 289 |
| Glycocoll. See Glycine | | - and vitamin B ₁₂ | 221 | Holmium, properties and isotopes | 91 |
| Glycocyamine, in urine | 288 | Haematuria | 291 | Homatropine, chemical data | 103 |
| Glycogen, in blood | 320 | Haemoglobin. See Methaemoglobin | | - effect on pupil | 357 |
| (See also Gluconeogenesis) | | Haemoglobin, biosynthesis, and copropor- | | - posology | 381, 410 |
| Glycoproteins, plasma | 314 | phyrin III | 338 | Homogentisic acid, in urine | 290 |
| Glycosides, international standards | 79 | - in erythrocytes | 337 | Hookworm | 167 |
| Glycosuria | 289 | - variation during growth | 333 | Hormones | 179 sq. |
| - and ACTH/adrenocortical hormones | 187 | - oxygen combining capacity | 331, 337 | - adrenocortical. See Corticosteroids | |
| - and insulin | 206 | - in plasma | 337 | - adrenocorticotrophic. See ACTH | |
| Glycotropic factor of anterior pituitary | 181 | - and specific gravity of blood (nomogram) | 304 | - of carbohydrate metabolism | 181 |
| Glyoxalase, in blood | 325 | - in urine | 291 | - cortical. See Corticosteroids | |
| Glyoxaline. See Iminazole | | Haemoglobinometers | 337 | - diabetogenic | 181 |
| Goat's milk anaemia, and folic acid | 220 | Haemoglobinuria | 291 | - follicle-stimulating | 179 |
| - and vitamin B ₁₂ | 222 | Haemogram of SCHILLING | 340 | - follicular. See Oestrogens | |
| Goitre and thyroxine | 208 | Haemolysis, and blood-group antigens | 342 | - galactopoietic | 180 |
| Gold, properties and isotopes | 93 | - and blood porphyrins | 338 | - glandotropic | 179 sq. |
| Gold-sol test, of spinal fluid | 353 | - and erythrocyte osmotic resistance | 310 | - gonadotropic | 179, 180 |
| Gonadotropic hormones | 179 | - and jaundice | 319 | - growth | 192, 193 |
| - international standards | 78 | - and plasma haemoglobin | 337 | - international standards | 78 |
| Gonorrhoea | 132 | - and spherocytes | 336 | - lactogenic | 180, 181 |
| Gout, and uric acid excretion | 288 | Haemolytic streptococci | 133 | - luteal. See Progesterone | |
| Grain | 55 | Haemometers | 337 | - luteinizing | 179 |
| Gram | 55 | Hafnium, properties and isotopes | 92 | - oestrogenic. See Oestrogens | |
| Gram atom | 75, 114 | Half-life, of artificial radio-isotopes | 98, 99 | - parathyroid | 207 |
| Gram equivalent | 75, 114, 297 | - of natural radio-isotopes | 84 sq. | - pituitary, anterior | 179 sq. |
| Gram mole. See Mole | | Halibut-liver oil, posology | 381 | - posterior | 194 |
| Gram-röntgen | 71 | Hand, secondary ossification centres | 268, 269 | - placental | 179 |
| GRAM's staining of bacteria | 129 sq. | HARRIS-BENEDICT basal metabolism standard | 246 | - sex | 201 sq. |
| Granulocytes, genealogy | 332 | Hb. See Haemoglobin | | - somatotropic | 192 |
| - neutrophil. See Neutrophils | | Head circumference of children | 257 sq. | - and spermatogenesis | 275 |
| - normal values, in blood | 339, 340 | Headache, ophthalmological | 364 | - steroid | 195 sq. |
| - in marrow | 340 | Heart, effect of adrenaline and noradrenaline | 206 | - chemistry | 195, 196 |
| Granuloma inguinale | 140 | - beef, chemical composition | 240 | - metabolism | 197 sq. |
| Grape sugar. See Glucose | | - blood pressure in | 302 | - urinary spectrum | 197 sq. |
| Gravitational constants | 79 | - chemical composition | 282 | - thyrotropic | 181 |
| Gravity, acceleration of | 79 | Heat, specific, of blood | 309 | HOWELL-JOLLY bodies | 33 |
| Greek alphabet | 7 | - units | 61 | HP (horse-power) | 6 |
| Growth, effect of ACTH/adrenocortical | | - transfer, coefficient of | 63 | HP. hr. (horse-power hour) | 6 |
| hormones | 188 | Height. See Body length | | Humour, aqueous (eye) | 36 |
| - basal metabolism in | 247, 248 | HEIM's pills, posology | 381 | - vitreous (eye) | 36 |
| - blood in, agglutinin titre | 342 | HEINZ inclusion bodies | 334 | Hundredweight | 5 |
| - erythrocytes | 335 | | | Hyaluronidase, in semen | 27 |
| - glucosamine | 320 | | | Hydnocarpus oil, posology | 308 |

Note that this index does not include the Supplement (pages 427-519).

This has been separately indexed on pages 520-528.

11-Ketoactianolone

Hydraemia

The following special indexes are also available:

Symbols and abbreviations for units page 50

Names and symbols of the elements page 83

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

H	page	H	page	I	page
Hydraemia, and erythrocyte count	335	Hypoglycaemia, effect of ACTH/adreno-cortical hormones	187	Iodine, properties and isotopes	90
Hydrargyrum. See Mercury		Hypokalaemia. See Hypopotassaemia		- protein-bound, and basal metabolism	244
Hydrastinine, Hydrastis, posology	381	Hypoparathyroidism, and vitamin D	211	- retention by thyroid	208, 282
Hydration, state of	295	Hypophoria	365	Iodoform, chemical data	103
Hydriodic acid, chemical data	104	Hypophysis. See Pituitary		- posology	382
Hydrobromic acid, chemical data	104	Hypopotassaemia, effect of ACTH/adreno-cortical hormones	187	Ionium, properties	96
Hydrochloric acid, chemical data	104	Hypothalamus, relation to pituitary	184	Ionogram, GAMBLE'S	296, 297
- in gastric juice	284 sq.	Hypothyroidism, and basal metabolism	244	Ipecacuanha, posology	382, 383, 410
- solutions, electrolytic data	118-120	Hz (Hertz, cycle per second)	59	Iridium, properties and isotopes	93
- posology	382			Iridocyclitis, ocular symptoms	364
- specific gravity	108			Iris	357
Hydrocortisone	203			Iritis, ocular symptoms	364
- chemistry	196			Iron, in blood	330
- function, etc.	182 sq.			- in breast milk	228
- metabolism	197			- in cow's milk	228
Hydrocyanic acid, chemical data	104			- in foods	230 sq.
- poisoning	426			- properties and isotopes	86
- posology	372, 374			- reduced, children's doses	411
Hydrogen, BOHR'S radius of atom	81			- salts, posology	380, 383, 409
- heavy. See Deuterium				- in urine	290
- isotopes, atomic weights and masses	80			Iron-deficiency anaemia. See under Anaemia	
- properties and isotopes	84			Isoagglutinins, ABO, variation with age	342
Hydrogen-ion concentration, of aqueous humour (eye)	362			Isoalloxazine	215
- of bile	283			Isoantigens	341
- of blood	308			Isoleucine. See <i>iso</i> Leucine	
- in acidosis and alkalosis	296, 297			Isoniazid, children's doses	410
- and carbonic acid/bicarbonate content	296, 297, 330			Isoprenaline sulphate, posology	383, 411
- of buffer solutions	105			Isosthenuria	299
- of cerebrospinal fluid	352			Isotonia with blood serum, calculation	115, 116, 296, 305
- at neck of cervix	276			- in infusion therapy	121
- of duodenum	283			Isotonic solutions, ammonium chloride	125
- of erythrocytes	335			- glucose	116, 117
- of faeces	287			- glucose-sodium chloride	116, 117, 124
- of gastric juice	284			- glucose-sodium chloride-sodium lactate	124
- of ileum	283			- sodium chloride	116, 117, 124
- ranges of indicators	106			- sodium chloride-sodium lactate	124
- of jejunum	283			- sodium lactate	124
- of lacrimal secretion	362			- RINGER'S	124
- of lens (eye)	363			Isotopes, natural	84 sq.
- of pancreatic juice	283			- radioactive, artificial. See Radio-isotopes	
- of prostate secretion	278				
- of saliva	283				
- of semen	276				
- and motility of spermatozoa	276				
- of urine	288				
- of vaginal secretion	276				
- of vitreous (eye)	364				
Hydrometer scales, conversion	109				
Hydromorphone. See Dihydromorphinone					
11-Hydroxyactianolone, structure	196, 197				
- in urine	200				
11-Hydroxyandrosterone, structure	196, 197				
- in urine	200				
β -Hydroxybutyric acid, in blood	322				
- conversion factors for acetone and	126				
- in urine	289				
17-Hydroxy-11-desoxycorticosterone	203				
- metabolism	198				
β -Hydroxyglutamic acid	224				
17-Hydroxyprogesterone, structure and metabolism	198				
1(-)-Hydroxyproline	224				
11-Hydroxy-steroids, structure and metabolism	197				
Hyoscyamine, chemical data	103				
- posology	382				
Hyoscyamus, posology	382				
Hyoscyne, chemical data	103				
- poisoning. See under Atropine	423				
- effect on pupil	357				
- posology	382, 410				
Hyperchromic erythrocytes	337				
Hypermetropia, Hyperopia	364				
Hyperostoses in vitamin-A poisoning	210				
Hyperphoria	365				
Hypertension	302				
Hyperthyreosis, and basal metabolism	244				
- and iodine retention by thyroid	208				
- and protein-bound iodine in blood	244, 329				
- and thyroxine	208				
Hyperthyroidism. See Hyperthyreosis					
Hyperventilation, and respiratory alkalosis	297				
Hypochromic erythrocytes	337				
- in infants	336				

Note that this index does not include the Supplement (pages 427-519).
This has been separately indexed on pages 520-528.

Mammary glands

11-Ketoactianolone (continued)

The following special indexes are also available:

Symbols and abbreviations for units page 50
Names and symbols of the elements page 83
Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

K	page
11-Ketoactianolone,	
- in corticosteroid metabolism	197
- in urine	200
11-Ketoactiocholanolone. See 11-Keto-actianolone	
11-Ketoandrosterone, chemistry	196
- in corticosteroid metabolism	197
- in urine	200
Ketogenic principle of anterior pituitary	181
α -Ketoglutaric acid, in blood	322
Ketone bodies. See Acetone bodies	
Ketonuria	289
11-Ketopregnanolone	196
11-Ketosteroids, metabolism	197
17-Ketosteroids	200
- effect of ACTH/adrenocortical hormones	182
- age changes	183
- chemistry	196
- in disease	183
- and eosinophil test of THORN	189
- metabolism	197, 198
- in urine	200
KEYS' formula for plasma oncotic pressure	296, 305
Kidd blood group	351
Kidneys, chemical composition	282
- clearance values	299, 300
- concentration capacity	299
- dilution test	288
- water loss via	296
Kilogram atom	75
Kilometer	52
Kilowatt	62
Kilowatt hour	61
Klebsiella	137
Knot (unit)	57
Kola extract, posology	383
KOLTHOFF's buffer solution	105
Krypton, properties and isotopes	88
KUSSMAUL's respiration in acidosis	297
Kynurenin, in biosynthesis of niacin	218
Kynureninase	217

L	page
lm (lumen)	72
lx (lux)	72
ly. (light year)	52
La (lambert)	72
Lab enzyme	284
Lacrimal secretion	362
Lactalbumin, in breast milk	228
- in cow's milk	228
Lactic acid, in aqueous humour (eye)	363
- in blood	322
- in cerebrospinal fluid	353
- chemical data	103, 104
- in gastric juice	284
- milk, preparation	411
- in semen	277
<i>Lactobacillus casei</i> factor	219
<i>Lactobacillus lactis</i> DORNER factor. See Vitamin B ₁₂	
<i>Lactobacillus leichmanni</i> factor. See Vitamin B ₁₂	
Lactoflavin. See Vitamin B ₂	
Lactogenesis	180
Lactogenic hormone	180
Lactose, in breast milk	228
- in urine	289
Lactosuria	289
Lactylphenetidine, posology	383
Laevulose. See Fructose	
Lambert	72
Lanatoside C, chemical data	103
- posology	383, 411
Lanthanum, properties and isotopes	90
Lauric acid, in breast milk	229
Lb. (pound weight)	60
Le antigens (blood group Lewis)	350
Lead, acetate, posology	383
- in blood, normal and tolerance levels	329
- compounds, chemical data	104
- in faeces	287
- in organs	282
- poisoning	329, 424
- , basophil granulated erythrocytes in	334

L	page
Lead, poisoning,	
- blood porphyrin in	338
- urine coproporphyrin in	291
- vitamin-D therapy	211
- properties and isotopes	94
Lecithin, in bile	283
- in blood	321
- conversion factors for lipid phosphorus and	126, 321
- international standards	78
Leishmaniasis	158
Length units	52
Lens of eye	363
Leptazol, posology	383, 411
Leptospirosis	150
L(-)-Leucine	224
- in breast milk	228
- in plasma	317
- of plasma proteins	315
- in urinary sediments	292, 293
- in urine	289
L(+)-isoLeucine	224
- in breast milk	228
- in plasma	317
- of plasma proteins	315
- in urine	289
Lethal dose, calculation	45
Leucocytes (See also Granulocytes, Lymphocytes, Monocytes, etc.)	339, 340
- classifications, ARNETH's and SCHILLING's	340
- cocarboxylase in	324
- distribution, age variations	333, 339
- shifts in	340
- genealogy	332
- total, age variations	333, 339
Leukaemia, leucocyte distribution in	340
Leukocytes. See Leucocytes	
Lewis blood group	350
LFT-systems of measurement	49
LH (luteinizing hormone)	179
LIEBERMANN-BURCHARD reactive steroids	321
Light, adaptation of pupil to	358
- mechanical and electrical equivalents	72
- units	72
- velocity in vacuum	80
Light year	52
Linseed, poisoning. See under Prussic acid	426
LINZENMEIER's blood sedimentation method	306
Lipase, in plasma	325
Lipids, in blood	321, 326
- and globulins	316
- in breast milk	228
- in cow's milk	228
- definition of neutral fats and	321
- in foods	230 sq.
- in lens (eye)	363
- metabolism, effect of ACTH/adrenocortical hormones	188
- effect of insulin deficiency	206
- phosphorus, in blood	326
- conversion factors for lipids and	126, 321
- in urine	289
Lipoproteins, in plasma	314, 316
Lipuria	289
Lithium, properties and isotopes	84
Lithosphere, abundances of elements	84 sq.
Litmus, indicator range	106
Litre	53
Liver, cells, effect of insulin	207
- chemical composition	282
- and jaundice	319
- injury, and amino-acid excretion	288
- and coproporphyrin excretion	291
- oils, and vitamin A	209
- and vitamin C	213
- and vitamin D	210
- poisoning by, and vitamin E	211
- and protein synthesis	315
LLD factor. See Vitamin B ₁₂	
LMT-systems of measurement	49
Lobeline, blood circulation time from	301
- posology	384, 411, 412
Logarithms, to the base 10	8 sq.
- calculation with	6
- to the base <i>e</i> (natural)	12 sq.
- of factorials	24
Lognormal distributions	34

L	page
<i>Lolium temulentum</i> , effect on pupil	357
Long-sightedness	364
LORAIN-LEVY syndrome	193
LOSCHMIDT's constant	79
- number	75, 79
Loudness units	7
Lu antigens (blood group Lutheran)	350
Lumbar fluid. See Cerebrospinal fluid	
Lumen (unit)	72
Luminal poisoning. See Barbiturates	423
Luminance units	72
Lunar constants	81
Lungs, chemical composition	282
- water loss through	295, 296
Lupus vulgaris, and vitamin D	211
Lutecium, properties and isotopes	92
Luteinizing hormone	179
Luteotropin	180
Lutheran blood group	350
Lux (unit)	72
Lymphatic tissue, effect of ACTH/adrenocortical hormones	188
Lymphocytes, in blood	339
- variations during growth	333
- in bone marrow	340
- genealogy	332
L(+)-Lysine	224, 225
- in breast milk	228
- in plasma	317
- of plasma proteins	315
- in urine	289
Lysozyme, in lacrimal secretion	362

M	
μ (micro-, symbol for millionth)	52
μ (micron, micrometre, μ m)	60
mb (millibar)	70
mc (millicurie)	75
mEq (milliequivalent)	76
mg% (milligram per cent)	75
mg.equiv (milliequivalent)	53
ml (millilitre)	75
mmol (millimole)	75
mol (mole)	52
m μ (millimicron, nanometre)	75
mval (milliequivalent)	69
M (maxwell)	7
M (mega, symbol for million)	115
M (molarity)	

Macrocytes	336
Macrocytic anaemia, and folic acid	220
- and vitamin B ₁₂	221
Macrocytosis	336
Macula lutea	359
MADDOX test for strabismus	365
Magnesium, in blood	327
- in body and organs	282
- in breast milk	228
- chloride, electrolytic data	118-120
- compounds, chemical data	104
- in cow's milk	228
- in faeces	287
- in foods	231 sq.
- hydroxide, electrolytic data	118-120
- in lens (eye)	363
- properties and isotopes	85
- in saliva	283
- sulphate, blood circulation time determined with	301
- electrolytic data	118-120
- trisilicate, posology	384
- in urine	290
Magnetic units	64 sq.
- polarization units	69
Magnetization units	68, 69
Magneton, BOHR's	81
- nuclear	81
Malachite green, indicator range	106
Malaria and chemotherapeutics	160
Male fern extract, posology	380, 384, 412
Malic acid, in blood	322
- chemical data	104
- in foods	231 sq.
Mammary glands, physiology	180

Note that this index does not include the Supplement (pages 427–519).
This has been separately indexed on pages 520–528.

Mammothropin

Nerves

The following special indexes are also available:

Symbols and abbreviations for units page 50

Names and symbols of the elements page 83

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172–178

M page

Mammothropin	180
Manganese, in blood	329
– in breast milk	228
– in cow's milk	228
– in foods	231 sq.
– in organs	282
– properties and isotopes	86
– sulphate, chemical data	104
MARCHIAFAVA-MICHELI syndrome	291
Marrow. See Bone marrow	
Mars, planetary constants	82
Mass numbers of natural isotopes	84 sq.
Mass units	55, 56
Mathematical constants	7
Mathematical tables, antilogarithms	10, 11
– <i>t</i> - and χ^2 -distributions	30
– exponential functions	17–20
– factorials	24
– logarithms	8–16
– normal distribution	25–30
– probabilities	29, 30
– probits	26–28
– squares and square roots	21–24
Maximal doses	367 sq.
MCH (mean corpuscular haemoglobin)	337
MCHC (mean corpuscular haemoglobin concentration)	337
McILVAINE's buffer solution	105
MCV (mean corpuscular volume)	335
Meal, test, EWALD. See EWALD test meal	
Means, arithmetical	32
– distribution of	38
Measurement, units of. See Units	
Meat, chemical composition	240 sq.
Medical prescriptions, notation	51
Medicaments. See Drugs	
Medina worm	166
Medomin, children's doses	412
Medulla, adrenal, and adrenaline	205, 206
Medulla oblongata, tumours, ocular symptoms	366
Mega- (symbol for million)	7
Mega-electron-volt	61
Megakaryocytes of bone marrow	340
Megaloblastic anaemias, and folic acid group	220
– and vitamin B ₁₂	221
Megalocytes, genealogy	332
Megohm	66
Melanogen, in urine	291
Mel B, international standard	79
Melting points of elements	84 sq.
Men, basal metabolism	246 sq.
– blood pressure	302
– blood sedimentation	306
– body water	295
– gonadotropin excretion	179
– height and weight	255
– nutritional requirements	226
– vital capacity	252
Menadione, Menaphthone. See Vitamin K	
Meningeomas, ocular symptoms	366
Meningitis, cerebrospinal	132, 137
Menstrual cycle, and basal metabolism	244
– and gonadotropins	179
– and oestrogens	202
– and pregnanediol excretion	202
– sex hormones in	204
– and thrombocytes	338
Menthol, chemical data	103
Mepacrine, chemical data	103
– and malaria	161
– posology	384, 413
Meperidine. See Pethidine	
Mepyramine maleate, posology	385
Mercaptalbumin, in plasma proteins	314
Mercurials, posology	385, 413
Mercury, planetary constants	82
Mercuric chloride, chemical data	104
– poisoning	425
– posology	385
Mercury, and compounds, posology	385, 413
– poisoning	425
– pressure unit (mm Hg)	61
– properties and isotopes	93
Mersalyl, posology	385, 413
Mesoinositol	223
Mesothorium (MsTh)	95

M page

Metabolic acidosis and alkalosis	296, 297
Metabolism, intermediary, products in blood	322
– of water and electrolytes	295 sq.
Metalddehyde poisoning	425
Metamycelocytes, in blood and bone marrow	340
Metanil yellow, indicator range	106
Methacholine chloride, posology	385
Methadone, posology	385
Methaemoglobin, in blood	338
– in urine	291
Methaemoglobinuria	291
Methanol. See Methyl alcohol	
L(–)-Methionine	224, 225
– in breast milk	228
– as methyl group donator	221, 222
– in plasma	317
– of plasma proteins	315
– in urine	289
Methoin, posology	386, 413
Methyl alcohol, chemical data	103
– poisoning	422
Methylatropine, posology	386
Methylene blue, chemical data	103
– posology	386
Methyl group donators	221, 222
Methylguanidine, in plasma	318
2-Methyl-1:4-naphthaquinone	212
N ¹ -Methylnicotinamide	217
Methyl orange, indicator range	106
Methylphenobarbitone, posology	386, 413
N ¹ -Methyl-2-pyridone-5-carboxylamide	218
Methyl red, indicator range	106
Methyl salicylate, posology	386
Methylsulphonal, posology	386
Methyltestosterone, posology	386
Methylthiouracil, posology	386
Methyl violet, indicator range	106
Metre	52
Metric Convention	49, 52, 55
Mendelevium	97
MeV (mega-electron-volt)	61
MICHAELIS' veronal buffer	105
Micro- (symbol for millionth)	7
Microcytes, Microcytosis	336
Micrometre, Micron	52
Micro-organisms, pathogenic. See Pathogenic organisms	
Midbrain tumours, ocular symptoms	366
Mil	52
Mile	52
Milk, breast, composition	228, 229, 240, 241
– secretion and ejection	180, 181
– cow's, composition	228, 229, 238, 239
– goat's, composition	240, 241
– sheep's, composition	240, 241
Milk teeth, development	271
Milky Way, constants	82
Millicurie	70
Millicurie of intensity	71
Milliequivalent	75
Milligram	55
Milligram equivalent	75, 114
Milligram per cent (not used in these Tables)	76
Millilitre	53
Millimetre	52
Mineralo-corticosteroids	203
Minim	54
Minute, of angle	57
– of time	56
MKS-system of measurement	49
MNSs blood group system	345
Molality, Molarity	75, 114
Molar volume, of carbon dioxide	120, 330
– of ideal gases	79
Mole	75, 114
Molecular weight, of electrolytes	118–120
– of medically important compounds	103
– of plasma proteins	314
Molecule, definition	114
MÖLLER-BARLOW disease, and vitamin C	213
Molybdenum, properties and isotopes	88
Moment, electric	66
– magnetic	68
Momentum, angular, BOHR's unit	81
Monilia, Moniliasis	168
Monocytes, in blood	339
– age variations during growth	333

M page

Monocytes, in bone marrow	340
– genealogy	332
Monoiodotyrosine	208
Moon, constants	81
Morel poisoning	425
Morphine (<i>See also Opium</i>), antidote	425
– chemical data	103
– poisoning	425
– posology	386, 413
– effect on pupil	357
Motility of spermatozoa	279 sq.
MSB, international standard	79
MTS-system of measurement	49
M.U. (mass unit)	55
Mucin, in bile	283
– in faeces	287
– in gastric juice	284
– in saliva	283
– in urine	292
Mucoproteins, in blood	314
– in lens (eye)	363
– in vitreous (eye)	364
Muscarine, Muscaridine, poisoning. See Mushrooms	
– effect on pupil	357
Muscles, cells, effect of insulin	207
– chemical composition	282
– ocular	355
Mushrooms, chemical composition	242
– poisoning	425
Mydriasis, Mydriatics	357
Myeloblasts, in blood and bone marrow	340
Myelocytes, in blood and bone marrow	340
– neutrophil, in blood	339
Myelogram of bone marrow	340
Myeloma, and BENCE-JONES proteinuria	288
Myohaemoglobinuria	291
Myopia, test-charts (inside back cover)	
Myosis, Myotics	357
Myristic acid, in breast milk	229
Myxoedema, and blood carotenes	208, 209
– and iodine retention by thyroid	208

N

n (nano-, symbol for 10 ⁻⁹)	7
nx (nox)	72
nm (nanometre)	52
N (newton)	59, 69
N (normality)	76, 114
Nanisme sénile	193
Nano- (symbol for 10 ⁻⁹)	7
Nanometre	52
Naperian logarithms, tables	12–16
Naphthalene, poisoning	425
– posology	386
Naphthol, posology	387
α -Naphtholphthalein, indicator range	106
β -Naphthol violet, indicator range	106
Narcophin, posology	387
Natrium. See Sodium	
Natural abundances of the elements	84 sq.
Natural logarithms, tables	12–16
Near-point of emmetropic eye	357
Near vision, test charts (inside back cover)	
Nemanthelminthes	165 sq.
– classification	171
Nematodes	165 sq.
Neoarsphenamine, international standard	79
– posology	387, 413
Neodymium, properties and isotopes	91
Neomycin	128 sq.
Neon, properties and isotopes	85
Neostibosan, children's doses	414
Neostigmine, chemical data	103
– posology	387, 414
Nephritis, glomerular, and hypertension	302
Neptune, planetary constants	82
Neptunium, properties and isotopes	97
Nerve, abducens	355
– oculomotor	355
– optic	360
– trochlear	355
Nerves, of the muscles of the eye	355
– of the skin, peripheral and radicular schemes (leaflets inside back cover)	

Note that this index does not include the Supplement (pages 427-519).
This has been separately indexed on pages 520-528.

pc (parsec)

Neuritis

Symbols and abbreviations for units page 50

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

Names and symbols of the elements page 83

N	page
Neuritis, optic, symptoms	364, 365
Neutral fats. See under Fats	
Neutrons, biological activity	71
- constants	80
Neutrophils, in blood	339
- classification	340
- variation with age	333, 339
Neutrophil myelocytes, in blood	339
Newborn, blood, erythroblasts	334
- erythrocyte count	335
- erythrocyte diameter	336
- erythrocyte haemoglobin	337
- erythrocyte osmotic resistance	310
- erythrocyte volume	335
- glucose	320
- haematocrit value	335
- haemoglobin	337
- α -keto-acids	322
- lactic acid	322
- leucocytes	339
- pH value	308
- proteins	313
- refractive index	307
- reticulocytes	334
- Rh factor	348
- thrombocytes	338
- body measurements	257
- eyeball, diameter	356
- pupillary diameter	357
- pupillary contraction	358
- faeces, stools per day	287
- gastric juice	285
- ophthalmoblenorrhoea of	132
- retrolental fibroplasia of	4, 31
- sodium and potassium metabolism, effect of ACTH	187
- urine, quantity and specific gravity	288
Newton (unit)	59
Niacin	217, 218
Nickel, properties and isotopes	87
Nicotinamide	217, 218
- methochloride	217
- posology	387
Nicotine, poisoning	425
Nicotinic acid	217, 218
- diethylamide. See Nikethamide	
- N-methylbetaine, urinary excretion	218
- nucleotides. See Pyridine nucleotides	
- posology	387
Night-blindness, and vitamin A	209
Nikethamide, chemical data	103
- replacement of niacin by	218
- posology	387, 414
Niobium, properties and isotopes	88
Niton. See Radon	
Nitric acid, chemical data	104
- solutions, specific gravity	107
Nitroamine, indicator range	106
Nitrogen, in blood, free	331
- non-protein	317
- in breast milk	228
- conversion factors for creatine, urea, etc. and	126
- in cow's milk	228
- in faeces	287
- in intestinal juice	283
- in lacrimal secretion	362
- metabolism, effect of ACTH/adrenocortical hormones	187
- effect of growth hormone	192
- non-protein. See Non-protein nitrogen	
- properties and isotopes	84
- in prostate secretion	278
- in saliva	283
- in urine	288
- in vitreous (eye)	364
Nitrogen mustard, chemical data	103
Nitrophenols, indicator ranges	106
Nitrous acid, chemical data	104
Nitrous fumes, poisoning by	425
Noise, equivalent pressures	73
Nomogram, for basal metabolism from age and calorie and oxygen consumption	249
- for blood haemoglobin from specific gravity	304
- for body surface of adults from weight and height	250

N	page
Nomogram,	
- for body surface of adults and children from weight and height (leaflet inside back cover)	
- for blood carbon dioxide distribution from total carbon dioxide and pH	330
- for plasma ionized calcium from total calcium and protein	328
- for Centigrade-Fahrenheit scales	58
- for erythrocyte haemoglobin from erythrocyte count and blood haemoglobin	337
- for haematocrit, from specific gravity of blood and plasma	304
- from viscosity of blood	306
- for male fertility from seminal data	280
- for plasma total bases from conductivity and protein content	308
- for plasma proteins from specific gravity	304
NONNE-APELT test	353
Non-protein nitrogen, of whole blood, corpuscles and plasma	317, 318
- of breast milk	228
- of cerebrospinal fluid	353
- of cow's milk	228
- of gastric juice	284
- of lacrimal fluid	362
- of lens (eye)	363
- of pancreatic juice	283
- of plasma	317, 318
- of prostate secretion	278
- of semen	277
- of vitreous (eye)	364
Noradrenaline, Norepinephrine	205
L(+)-Norleucine	224
Normal body measurements during growth	256 sq.
Normal distribution	35 sq.
- areas and ordinates, table	25
- percentile division	256
- normal probability integral	29
- probability ranges, calculation	37
- probability table	29
- probit transformation	44
- table of probits	26-28
Normal solution, definition	76, 114
0.1-Normal solutions of reagents	104
Normal volume, of carbon dioxide	120, 330
- of ideal gases	79
Normoblasts, in bone marrow	340
Normochromic erythrocytes	337
Normocytes, in blood	336
L(+)-Norvaline	224
Novocain. See Procaine	
Nox	72
NPN. See Non-protein nitrogen	
N.T.P., correction of gas volumes to	127
Nubecula of urine	291
Nucleoproteins of lens (eye)	363
Nucleotides, in blood	318, 324
- nitrogen of	317
- phosphorus of	326
- flavine-adenine (vitamin-B ₂)	216
- in blood	324
- pyridine	218
- in blood	318, 324
Nucleotide pentoses, in blood	320
Null hypothesis	38
Numerical eccentricity of erythrocytes	336
Nuts, chemical composition	236, 237
Nutrient intake, and intraocular pressure	362
- requirements, daily	226
Nutritional factor X. See Vitamin B ₁₂	
Nux vomica (See also Strychnine), posology	387, 414
Nyxolan, children's doses	414

O

O	page
Ω (ohm)	66
osm (osmole)	114
Oblique muscles of eye, pareses	355
Obstetric norms	275
Occipital lobe tumours, and ocular symptoms	365
Octadecaenoic acids, in breast milk	229
Octave	74
Ocular muscles	355

O	page
Ocular symptoms, and brain tumours	365
Oe (oersted)	67
Oedema, papillary	365, 366
OEHLER's blood test	342
Oersted	67
Oestradiol. See under Oestrogens	
Oestrane, structure and derived steroids	190
Oestriol. See under Oestrogens	
Oestrogens,	201
- functions	204
- chemistry	190
- metabolism	199
- posology	387, 388
Oestrone. See under Oestrogens	
Ohm	64, 66
Oidiomycosis	168
Oils, edible, chemical composition	238, 239
Old tuberculin. See Tuberculin, old	
Oleic acid, in breast milk	229
Olfactory meningeoma, and ocular symptoms	366
Oligospermia	279
Oliguria	288
Oncotic pressure. See Colloid-osmotic pressure	
Opacity reference preparation, international standard	70
Ophthalmoblenorrhoea of newborn	132
Ophthalmological headache	366
Opiates, poisoning	421
Opium, posology	388, 389, 411
Optic nerve	366
Orbit (eye)	355
Organs, chemical composition	287
- weight	10
Organisms, pathogenic. See Pathogenic organisms	
L(+)-Ornithine	22
Orthocaine, posology	387
Osmium, properties and isotopes	9
Osmolality	11
- of various electrolytes	11
- and freezing-point depression	11
- of glucose and salt solutions	11
- of serum	116, 29
Osmolarity	11
- of infusion solutions	124, 12
- and specific gravity of urine	29
Osmotic coefficient, definition	11
- of glucose and salt	11
Osmotic concentration. See Osmolality and Osmolarity	
Osmotic pressure, of aqueous humour (eye)	36
- calculation	115, 11
- of lens (eye)	36
- of plasma and serum	115, 116, 296, 30
- of vitreous (eye)	26
Osmotic relations of body fluids	29
Osmotic resistance of erythrocytes	31
Ossification centres, secondary	268
Quabain, chemical data	10
- posology	389, 411
Ounce	54, 5
OWREN's blood coagulation theory	31
Oxalic acid, chemical data	10
- in foods	231
- poisoning. See under Acids	
- in urine	28
Oxidation enzymes	215, 21
Oxophenarsine, children's doses	41
- international standard	7
Oxy-. See Hydroxy-	
Oxygen, in blood	330, 33
- and haemoglobin content	33
- consumption for proteins, fats and carbohydrates	24
Oxytetracyclin	128
- posology	389, 411
Oxytocin	19
- posology	38

P

P	page
π , value of	
p (pico-, symbol for 10^{-12})	
p (pond)	
pc (parsec)	52, 3

Note that this index does not include the Supplement (pages 427-519).

This has been separately indexed on pages 520-528.

Potassium

ph (phot)

The following special indexes are also available:

Symbols and abbreviations for units page 50

Names and symbols of the elements page 83

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

P	page
ph (phot)	72
pH. See Hydrogen-ion concentration	
pz (pièze)	60
P (poise)	63
P (probability)	29, 30
P, vitamin	214

Packed cell volume (PCV). See Haematocrit value	
Pain threshold, acoustic	73
Palladium, properties and isotopes	89
Palmitic acid, in breast milk	229
Pamaquin, posology	389, 415
Pancreas, chemical composition	282
- diseases, and blood amylase	324
Pancreatic juice	283
- electrolytes	298
PANDY'S test	353
Pantothenic acid	216
Papaverine, chemical data	103
- blood circulation time measured with	301
- posology	389, 415
Papillary oedema	365, 366
Para-aminobenzoic acid	219
Para-aminohippurate clearance, renal	300
Para-aminosalicylic acid, posology	389
Paraldehyde, posology	389
Parallax, solar	81
Paralysis, of ocular muscles	355
- pupillary	359, 360, 365
Parasites	157 sq.
Parathyroid hormone	207
Paratyphoid	138
Pareses of ocular muscles	355
Parietal lobe tumours, and ocular symptoms	365
Pars plana, Pars plicata (eye)	357
Parsec	52, 82
Parturition. See under Pregnancy	
PAS. See Para-aminosalicylic acid	
Pathogenic organisms, and antibiotics	128
- characteristics	129 sq.
- classification	169 sq.
- index of diseases and	172 sq.
PCV (packed cell volume). See Haematocrit value	
Peck (unit)	54
Pellagra, and folic acid	220
- and nicotinic acid	218
Pelvic breadth, during growth	257 sq.
Pelvimetry	275
Penicillin	128 sq.
Penicillin G, posology for children	405
Penicillin G sodium, chemical data	103
- international standard	79
Penicillin K sodium, international standard	79
Pennyweight	55
Pentaquine, posology	389
Pentetrazole. See Leptazol	
Pentobarbitone, chemical data	103
- sodium, posology	389
Pentoses, in plasma	320
- in urine	289
Pentothal. See Thiopentone	
Pepsin, in gastric juice	284
Peptide-nitrogen of plasma proteins	315
Percentile division	256
Period, of moon	81
- of planets	82
Periodic system of elements	82
Peripheral cutaneous nerves	
(leaflet inside back cover)	
Permeability, absolute	64, 68, 80
Permittivity, absolute	64, 65, 80
Pernicious anaemia, and citrovorum factor	220
- and coproporphyrin in urine	291
- and gastric juice	286
- and vitamin B ₁₂	221
Pethidine, chemical data	103
- posology	389
Petroleum spirit, poisoning	425
Phaeochromocytoma, and adrenaline	206
PHARMACOPOEA GALICA, usual doses	367 sq.
PHARMACOPOEA HELVETICA, maximal doses	367 sq.
PHARMACOPOEA INTERNATIONALIS, international standards	77 sq.
- posology	367 sq.

P	page
Phenacetin, chemical data	103
- poisoning	422
- posology	390, 416
Phenazone, chemical data	103
- poisoning	422
- posology	370, 416
Pheniodol, posology	390
Phenobarbitone, chemical data	103
- and sodium salt, posology	390, 416
Phenol, posology	390
Phenols, in blood	318
- in urine	288
Phenolphthalein, indicator range	106
- posology	390
Phenol red, indicator range	106
- posology	391
Phenolsulphatase, in plasma	325
Phenolsulphonphthalein. See Phenol red	
Phenotypes of blood groups	344 sq.
L(-)-Phenylalanine	224, 225
- in breast milk	228
- in plasma	317
- of plasma proteins	315
- in urine	289
Phenylbutazone, posology	391
Phenylchromone, vitamin-P activity	214
Phenylephrine tartrate, children's doses	419
Phenyl salicylate, posology	393, 417
Phenytoin (diphenylhydantoin), chemical data	103
- posology	391, 416
Phloretin, vitamin-P activity	214
Pholedrine, children's doses	417
Phon	73
Phosgene poisoning	426
Phosphatase, in plasma	325
- in prostate	278
- in semen	278
- SHINOWARA'S unit	325
Phosphates. See Phosphorus	
Phosphatides. See Phospholipids	
Phosphaturia	290
Phospholipids, in blood	321
- in organs	282
- in plasma protein fractions	314
Phosphoric acid, chemical data	104
- solutions, specific gravity	108
Phosphorus, in aqueous humour (eye)	363
- in blood	326
- in bone	282
- in brain	282
- in breast milk	228
- in cow's milk	228
- daily requirement	227
- in various electrolytes	118-120
- in faeces	287
- in foods	231 sq.
- in heart	282
- in infusion solutions	124, 125
- inorganic, conversion factors for phosphates and	120
- in intestinal juice	283
- in intestine	282
- in kidneys	282
- in lens (eye)	363
- in liver	282
- in lungs	282
- metabolism, and vitamin D	210
- in muscle	282
- in organs	282
- in pancreas	282
- posology	391
- properties and isotopes	85
- in prostate secretion	278
- in semen	277
- serum, inorganic, and growth	193, 326
- in skin	282
- in spleen	282
- in thyroid	282
- in urinary sediments	292, 293
- in urine	290
Phosphorylated pentoses, in plasma	320
Phot	72
Photometric units	72
Physical constants	79 sq.
- qualities, definition	49
- scale of atomic weights	80

P	page
Physostigmine (eserine), chemical data	103
- poisoning	422
- posology	391
- effect on pupil	357
Phytin	223
Pico- (symbol for 10 ⁻¹²)	7
Picric acid, indicator range	106
Picrotoxin, in barbiturate poisoning	423
- chemical data	103
- posology	391
Pilocarpine, chemical data	103
- poisoning	422
- posology	391
- effect on pupil	357
Pinealoma, ocular symptoms	366
Pint	54
Piperocaine, chemical data	103
Pituitary, activity and morphological changes	185
- anterior, hormones	179 sq.
- dwarfism and gigantism	193
- posterior, hormones	194
- international standard	78
- posology	391
- tumours, and ocular symptoms	365, 366
Pituitary-adrenal system	184 sq.
Placenta, substances with ACTH-activity from	182
- gonadotropic hormones of	179
- oestrogens of	202, 204
- progesterone of	202, 204
Plague, and antibiotics	140
PLANCK'S quantum	62, 80
- radiation constants	81
Planetary constants	82
Plasma, composition and physical properties.	
See under Blood	
Plasma minute-volume	300
Plasma proteins (See also under Proteins)	313 sq.
Plasmacytes, in bone marrow	340
- genealogy	332
Plasminogen	314
Plasmocytes. See Plasmacytes	
Plasmodia	160
Platelets, blood. See Thrombocytes	
Platinum, properties and isotopes	93
Platyhelminthes	161 sq.
- classification	171
Plumbum. See Lead	
Pluto, planetary constants	82
Plutonium, properties and isotopes	97
Pneumonia. See Disease index	
Pneumococcus	133
- antisera, international standards	77
Podophyllum resin, posology	391
Poikilocytes, Poikilocytosis	336
POIRRIER'S blue, indicator range	106
Poise (unit)	63
Poisoning, (symptoms and treatment)	422 sq.
- by dicoumarol derivatives	213
- by vitamin A	210
- by vitamin D	210
Polarization, dielectric	66
- magnetic	69
Poliomyelitis	154
Polonium, properties and isotopes	94
Polychromatic erythrocytes	334
Polychromatophilia	334
Polycythaemia vera, and blood viscosity	306
- and blood volume	305
Polymorphonuclear leucocytes	340
Polymyxin	128 sq.
Polysaccharides, in plasma	320
Polyuria	288
Poncelet	62
Pond	59
Pons, tumours, ocular symptoms	366
Porphyria, in blood	338
- in urine	291
Posology, adult	367 sq.
- in infancy and childhood	401 sq.
Potassium, in bile	298
- in blood (fresh)	297, 327
- in blood (preserved)	123
- in body and organs	282
- in bone	282
- in brain	282
- in breast milk	228
- in caecostomy secretion	298

Note that this index does not include the Supplement (pages 427-519).
This has been separately indexed on pages 520-528.

Radioactive disintegration

Potassium (continued)

The following special indexes are also available:
Symbols and abbreviations for units page 50
Names and symbols of the elements page 83
Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

P page

Potassium, 353

- in cerebrospinal fluid 353

- compounds, chemical data 104

- - posology 392, 417

- in cow's milk 228

- deficiency 122

- dichromate, chemical data 104

- - poisoning 424

- in erythrocytes 327

- in faeces 287, 298

- in foods 231 sq.

- in gastric juice 298

- gluconate, electrolytic data 118

- in heart 282

- hydroxide, chemical data 104

- - solutions, specific gravity 110

- in ileal secretion 298

- in intestinal juice 298

- in intestine 282

- in kidneys 282

- in lacrimal secretion 362

- in lens (eye) 363

- in liver 282

- in lungs 282

- metabolism, effect of ACTH/adreno-cortical hormones 187

- in muscle 282

- oxide, electrolytic data 118

- in pancreas 282

- in pancreatic juice 298

- permanganate, chemical data 104

- in plasma 327

- properties and isotopes 86

- in prostate secretion 298

- replacement therapy, parenteral 122 sq.

- in saliva 298

- salts, electrolytic data 118-120

- in serum 297, 327

- in serum ultrafiltrate, serum water 298

- in skin 282

- in sweat 298

- in transudates 298

- in urine 290, 299

- in uterus 282

Potential, electric 64

- magnetic 67

Poultry, chemical composition 240 sq.

Pound 55

Power units 62

POYNTING'S vector 69

Pp blood group system 345

Praseodymium, properties and isotopes 91

Pregnancy (and puerperium), anaemias of 220-222

- basal metabolism 248

- blood values 272

- breast milk, composition 228, 229

- colostrum 228, 229

- gonadotropin secretion 179

- incompatible 348

- mammary glands and lactogenic hormone 180, 181

- nutritional requirements 226

- obstetric norms 275

- plasma proteins 273

- plasma volume and water balance 272

- sex hormones 204

- tests 179

- urinary oestrogens 202

- urinary pregnanediol 202, 203

- uterus, development and involution 274

- weight increase 272

Pregnane, structure and derived steroids 196

alloPregnane, structure and derived steroids 196

Pregnanediol 202, 203

- chemistry 196

- metabolism 199

alloPregnanediol, 202

- chemistry 196

- metabolism 199

Pregnanedione 196

Pregnanol 196

Pregnanolones 196

Pregnenetriolone 196

Pregnenolone 196

Presbyopia, correction 357

- and headache 361

Prescriptions, notation 54

P page

Pressure, intraocular 362

Pressure units 60

Primaquine, posology 392

Probabilities, calculation 36 sq.

- tables 29, 30

Probits, table of 26-28

Probit transformation 44

Procaine, chemical data 103

- poisoning 424

- posology 392, 417

Procaine benzylpenicillin, posology 392

Proerythroblasts, in bone marrow 340

Profibrinolysis, in plasma 325

Progeria 193

Progesterone 202

- chemistry 196

- function 204

- metabolism 199

- posology 392

- international standard 78

Progranulocytes, in bone marrow 340

Proguanil, posology 392

Prolactin 180

- international standard 78

L(-)-Proline 224

- in plasma 317

- of plasma proteins 315

- in urine 289

Promethazine, posology 393

Promethium, properties and isotopes 91

Promyelocytes, in blood 340

Propyl red, indicator range 106

Propylthiouracil, posology 393

Prostate 278

- secretion 278

Prostigmine, effect on pupil 357

Protamine, international standard 78

Protanomalia, Protanopia

(test charts inside back cover)

Proteins, in aqueous humour (eye) 363

- in breast milk 228

- - amino-acid composition 229

- in cerebrospinal fluid 352, 353

- conversion factors for protein nitrogen and 126

- in foods 230 sq.

- - amino-acid composition 225

- in intestinal juice 283

- in lacrimal secretion 362

- in lens (eye) 363

- metabolism, effect of ACTH/adrenocortical hormones 187

- - and calorific value 245

- - and blood creatine level 318

- - effect of growth hormone 192

- - and insulin 206

- - water of oxidation 295

- - effect of testosterone 187, 204

- - and blood urea level 317

- nutritional requirements, daily 226, 227

- in pancreatic juice 283

- plasma and serum 313 sq.

- - and bilirubin 314, 319

- - nomogram for blood calcium from 328

- - and copper 314

- - and electrical conductivity 308

- - fractionation 313 sq.

- - and iodine 314, 319

- - ionized, conversion factors for 120, 297

- - and iron 314

- - and lipids 314, 316

- - and oncotic pressure 296, 305

- - in pregnancy 272 sq.

- - and sedimentation rate 307

- - and serum specific gravity 304

- - and plasma viscosity 306

- - and total plasma volume 316

- - and serum water content 114, 295

- in prostate secretion 278

- in semen 277

- in urine 288

- - routine tests 294

Proteinuria, BENCE-JONES, and myeloma 288

Prothrombin 314

Prothrombinopenia, and vitamin K 212

Prothrombin time 310

Protoactinium, properties and isotopes 96

Protons, biological activity 71

P page

Protons, constants 8

Protoporphyrin, in blood 33

- in urine 29

Prototype kilogram 5

- metre 5

Protozoa 157 sq.

- classification 1

Provitamin A. See Carotenes

- D₂. See Ergosterol

- D₃. See 7-Dehydrocholesterol

- D₄. See 22-Dihydroergosterol

- D₅. See 7-Dehydrositosterol

Prussic acid. See Hydrocyanic acid

PS (horse-power) 6

PSH (horse-power hour) 6

Pseudoglobulins 31

Pseudomonas 12

Psittacosis 15

Pteroylglutamic acids. See Folic acid

Pteroylglutamic acid conjugase, 22

- in blood 32

Puerperium. See under Pregnancy

Pulmonary blood pressure 30

Pulse, and intraocular pressure 36

Pupil 357 sq.

- paralyses 36

- reflex pathways 36

Pupillometer light adaptation 35

Purine derivatives, in blood 31

- in foods 231 sq.

- in urine 28

Pyramidone poisoning. See under Aniline 42

Pyridine nucleotides 21

- in blood 31

Pyridoxal, Pyridoxamine, Pyridoxic acid, Pyridoxine 21

Pyruvic acid, in blood 32

- in cerebrospinal fluid 35

- and vitamin B₁ 214, 32

Q

q. (quintal) 5

Q fever 15

- antiserum, international standard 7

Quadratic deviation and variation, mean 3

Qualities, physical, definition 4

Quantum, PLANCK'S 62, 8

Quart 5

QUECKENSTEDT test 35

QUICK'S blood coagulation theory 31

- prothrombin time determination 31

Quinacrine. See Mepacrine

Quinidine, chemical data 10

- sulphate, posology 39

Quinine, chemical data 10

- posology 393, 41

Quintal 5

R

r (röntgen) 7

rad (radiation unit) 7

r.b.e. (relative biological effectiveness) 7

rem (röntgen-equivalent-man) 7

rep (röntgen-equivalent physical) 7

°R (degree Réaumur) 5

Rachitis. See Rickets

Radian 5

Radiation, constants 8

- corpuscular, units 7

- doses, maximum permissible 71, 99, 10

- gamma. See Gamma rays

- of artificial isotopes, biological uses 98 sq.

- of natural isotopes 84 sq.

- solar 8

- units 70, 7

- X-. See X-rays

Radicular cutaneous nerves

(leaflet inside back cover)

Radioactinium (RdAc), properties 9

Radioactive disintegration, of artificial iso-topes 9

- of natural isotopes 84 sq.

- units 70, 7

Note that this index does not include the Supplement (pages 427-519).

This has been separately indexed on pages 520-528.

Sodium chloride

Symbols and abbreviations for units page 50

Names and symbols of the elements page 83

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

Radioactive isotopes

R	page
Radioactive isotopes. See Radio-isotopes	
Radio-isotopes, artificial, in biology and medicine	98 sq.
- dose rates	100
- dosimetry	99
- nuclear data	98, 99
- uses	101, 102
Radiothorium (RdTh), properties	96
Radium, properties and isotopes	95
Radium-A, -B, -C, -C', -D, -E, -F	94
Radium-C" and -E"	93
Radium emanation. See Radon	
Radon, properties and isotopes	95
- as radioactivity unit	70
<i>Rana pipiens</i> test for gonadotropins	179
° Rank. (degree Rankine)	56
Rat-bite fever	130, 142
α-Rays. See Alpha rays	
β-Rays. See Beta rays	
γ-Rays. See Gamma rays	
RBC (red blood count)	335
Reagents, buffering	105
- pH indicator	106
- solutions, 0.1-normal	104
- - specific gravity	107 sq.
- for urine tests	294
Réaumur temperature scale	57
Rectus muscles of eye, pareses	355
Red blindness, test charts (inside back cover)	
Red blood cells. See Erythrocytes	
Red blood count (RBC)	335
Red-green blindness, test charts (inside back cover)	
"Red" hypertension	302
Reducing substances, in aqueous humour (eye)	363
- in blood	320
- in cerebrospinal fluid	353
- definition	289
- in lacrimal secretion	362
- in lens (eye)	363
- in prostate secretion	278
- in semen	277
- in urine	289
- - tests for	294
- in vitreous (eye)	364
Reductase, cytochrome C	216
Reference preparations, international biological	77 sq.
Refractive index, of aqueous humour (eye)	362
- of cerebrospinal fluid	352
- of cornea	356
- of lens (eye)	363
- of plasma	307
- of vitreous (eye)	364
Register ton	54
Regression, statistical	42
Relapsing fever	148, 149
Relative abundances of elements	84 sq.
Relative biological effectiveness	71
Renal clearance	300
- function values	299, 300
- hypertension	302
- water loss	295, 296
Resistance, electrical	66
Resorcinol, chemical data	103
- posology	393
Respiration, and pupillary diameter	358
- and vital capacity	251
Respiratory acidosis and alkalosis	296, 297
- quotient	244
- - and growth hormone	192
- - and fat and carbohydrate consumption	245
- enzyme, WARBURG'S	215, 216
- volume	251
Retention jaundice	319
Reticulocytes	334
- genealogy	332
- variation during growth	333
- and coproporphyrin	338
Reticulo-endothelial system, and blood regeneration	319
- and genealogy of blood corpuscles	332
Reticulum cells, in bone marrow	340
Retina	359
Retinenes	209
Retrolental fibroplasia	4, 31
Rh (Rhesus) blood group	346 sq.

R	page
Rhenium, properties and isotopes	92
Rhesus blood group	346 sq.
Rhizopterin	219
Rhodium, properties and isotopes	89
Rhodopsin (visual purple), and vitamin A	209
Riboflavin. See Vitamin B ₂	
Ribonucleic acid, of plasma	318
Rickets, and alkaline phosphatase in blood	325
- and inorganic phosphorus in blood	326
- and phytin in foods	223
- and vitamin D	211
Rickettsia	151
RINGER'S infusion solutions	124
Rochelle salt, chemical data	103
Rods and cones, retinal	359
Röntgen (unit)	70
Röntgen-equivalent-man	71
Röntgen-equivalent physical	71
Röntgen rays. See X-rays	
Rosolic acid, indicator range	106
ROTHERA'S test	294
Roundworms. See Nematodes	
Roundworm (Ascaris)	168
RQ. See Respiratory quotient	
Rubidium, properties and isotopes	88
Ruthenium, properties and isotopes	89
Rutin	214
- chemical data	103
Ry (rydberg)	61
RYDBERG constant	81

S	page
σ (standard deviation)	32
sb (stilb)	72
sk (skot)	72
sn (sthene)	59
S (Siemens)	67
Sabina, posology	393
Saccharin, blood circulation time determined with	301
Saccharose. See Sucrose	
Sal ammoniac poisoning	422
Salicylates, poisoning	426
- - and hyperventilation	297
Salicylic acid, chemical data	103
Saline. See under Sodium chloride	
Saliva	283
- electrolytes	298
Salmonella	138, 139
Salol, posology	393, 417
Salt. See Sodium chloride	
Salt retention, effect of ACTH/adrenocortical hormones	187
Samarium, properties and isotopes	91
Samples, statistical treatment	38 sq.
Santonin, chemical data	103
- poisoning	426
- posology	393, 417
Sarcosine	224
Saturn, planetary constants	82
SAYERS' ascorbic acid test for ACTH	182
Scandium, properties and isotopes	86
Scarlet fever	133
- streptococcus antitoxin, international standard	77
SCHARDINGER'S reductase	216
SCHICK test, effect of ACTH/adrenocortical hormones	188
- toxin, international standard	78
SCHILLING'S haemogram and leucocyte classification	340
Schistosomiasis	162
Schizomycetes. See Bacteria	
Sclera	356
Scopolamine. See Hyoscine	
Scotopic vision, photometric units for	72
Scruple	55
Scurvy, and vitamin C	213
S.D. (standard deviation)	32
Sea foods, chemical composition	242, 243
Seatworm	168

S	page
Second (angle)	57
- (time)	56
Secondary ossification centres	268 sq.
Secretions, intestinal	283, 298
Secretor/non-secretor system	341, 351
S.E.D. (skin erythema dose)	70
Sediments, urinary	292, 293
Sedimentation of blood	306, 307
- constant of plasma proteins	315
- rate. See under Erythrocytes	
SEEGERS' blood coagulation theory	312
Segmented neutrophils	340
Selenium, properties and isotopes	87
Self-inductance	69
Semen, chemical and physical data	276 sq.
- ejaculate volume	276
- prostate secretion in	278
- spermatozoa in	279 sq.
L(-)-Serine	224
- in plasma proteins	315
Serum (See also under Blood)	
- proteins. See under Proteins	
- ultrafiltrate, electrolytes	298
- water, electrolytes	298
- - and serum protein content	114, 295
- - and serum specific gravity	303
Sex hormones. See under Hormones	
Shigella	139, 140
SHINOWARA'S phosphatase unit	325
Shipping ton	54
SHOCK standard for basal metabolism	247
Short sight. See Myopia	
Sickle cells	336
Sickle-cell anaemia	336
Sidereal time and units	56, 81
SIEGBAHN'S X-unit	52
Siemens (unit)	67
SIEVERT dose	71
Significance, statistical	38 sq.
Silicon, in blood	327
- in lens (eye)	363
- properties and isotopes	85
Silver, nitrate, chemical data	104
- - posology	394
- in organs	282
- properties and isotopes	89
- protein, posology	394
SIMMONDS' disease	189
Siriometre	52
Sirius, distance of	52
Sitting height in childhood and adolescence	257 sq.
Skeleton, chemical composition	282
- development	268 sq.
Skin, chemical composition	282
- innervation schemes (leaflets inside back cover)	
- water loss through	295, 296
Skin erythema dose	70
Skot	72
SLR factor	219
Smallpox	153
SMYTHE factor	55, 80
Snake-bite	426
SNELLEN'S formula for visual acuity (test chart inside back cover)	
Sodium, acetate, electrolytic data	118-120
- acetylarsanilate, posology	394
- p-aminosalicylate, electrolytic data	118-120
- arseniate, posology	394
- bicarbonate, chemical data	104
- - children's doses	418
- - in alkali loading test	288
- - electrolytic data	118-120
- - isotonic solutions	125
- in blood (fresh)	297, 327
- in blood (preserved)	123
- in body and organs	282
- in bone	282
- in brain	282
- in breast milk	228
- bromide, electrolytic data	118-120
- - posology	394, 418
- cacodylate, posology	394
- in caecostomy secretion	298
- chloride, in cerebrospinal fluid	353
- - chemical data	104
- - electrolytic data	117-125

Note that this index does not include the Supplement (pages 427-519).

This has been separately indexed on pages 520-528.

Syneresis

Sodium chloride (continued)

The following special indexes are also available:

Symbols and abbreviations for units page 50

Names and symbols of the elements page 83

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

S	page	S	page	S	page
Sodium, chloride,		Specific gravity,		Stokes (unit)	63
- - infusion solutions with glucose, sodium		- of bile	283	Stomach emptying time	286
lactate and	124	- of blood	303	Stools, daily, in infancy	287
- - osmotic coefficient	117	- - nomogram for haematocrit, haemoglobin		Stoppani hydrometer scale	107
- - radioactive, blood circulation time		and proteins from	304	Strabismus, latent	364, 365
determined with	301	- of breast milk	228	Stramonium, posology	395
- - daily requirement	227	- of calcium chloride solutions	109	Streptococci	133, 134
- - retention, effect of ACTH/adrenocortical		- of cerebrospinal fluid	352	Streptomycin, chemical data	103
hormones	187	- of colostrum	228	- international standard	79
- - solutions, specific gravity	109	- of cow's milk	228	- and pathogenic organisms	128 sq.
- citrate, electrolytic data	118-120	- definition	60	- posology	396, 419
- - posology	394, 418	- of elements	84 sq.	- toxicity	128
- acid citrate, electrolytic data	118-120	- of erythrocytes	335	Stress	185
- compounds, chemical data	104	- of ethyl alcohol solutions	111 sq.	Strontium, properties and isotopes	88
- in cow's milk	228	- of eyeball	356	Strophanthin-G. See Ouabain	
- in faeces	297, 298	- of ferric chloride solutions	108	Strophanthin-K, posology	396, 419
- in foods	231 sq.	- of gastric juice	284	Strychnine (<i>See also Nux vomica</i>), chemical	
- in gastric juice	298	- of glycerol solutions	111	data	103
- glycocholate, in blood	321	- of hydrochloric acid solutions	108	- poisoning	426
- in heart	282	- of lens (eye)	363	- posology	396, 419
- hydroxide, chemical data	104	- of nitric acid solutions	107	Sublimate, corrosive. See Mercuric chloride	
- - solutions, specific gravity	110	- of pancreatic juice	283	Succinic acid, chemical data	104
- in ileal secretion	298	- of phosphoric acid solutions	108	- in plasma	322
- indigodisulphonate, indicator range	106	- of plasma	303	Sugars. See Fructose, Glucose, Reducing	
- in intestinal juice	298	- of potassium hydroxide solutions	110	substances, Sucrose, etc.	
- in intestine	282	- of prostate secretion	278	Sugar metabolism. See Carbohydrate	
- iodide, posology	395, 418	- of saliva	283	metabolism	
- in kidneys	282	- of semen	277	Sulpharsphenamine, international standard	79
- in lacrimal secretion	362	- of serum	303	- posology	397
- lactate, electrolytic data	118-120	- - and protein content	304	Sulphates, conversion factors for sulphur and	
- in lens (eye)	363	- of serum water	303	electrolytic data	118-120
- in liver	282	- of sodium chloride solutions	109	Sulphonamides, chemical data	103
- in lungs	282	- of sodium hydroxide solutions	110	- posology	396, 397, 419
- metabolism, effect of ACTH/adrenocortical		- of sodium sulphate solutions	109	- as urinary sediment	292, 293
hormones	187	- of sodium thiosulphate solutions	108	Sulphosalicylic acid test for urinary protein	294
- in muscle	282	- of sucrose solutions	110	Sulphur, in blood	322
- nitrite, posology	395	- of urine	288, 299	- in body and organs	282
- oxide, electrolytic data	118	- of vitreous (eye)	363	- in breast milk	228
- in pancreas	282	Specific heat of blood	309	- conversion factors for sulphates and	
- in pancreatic juice	283, 298	Specific surface of erythrocytes	336	- in cow's milk	228
- phosphate, electrolytic data	118-120	Spectral sensitivity of eye	72	- in faeces	287
- acid phosphate, electrolytic data	118-120	Spectroscopic unit, X-ray	52	- in foods	231 sq.
- properties and isotopes	85	Spermatozoa	279 sq.	- in lens (eye)	363
- salicylate, electrolytic data	118-120	Spermene, in prostate	278	- in plasma proteins	315
- - posology	395, 418	- in semen	277	- properties and isotopes	85
- in saliva	298	Sphenoid wing meningioma, ocular		- in saliva	283
- in serum ultrafiltrate, serum water	298	symptoms	366	- trioxide, chemical data	104
- in skin	282	Spheroocytes, Spherocytosis	336	- in urine	290, 299
- sulphate, electrolytic data	118-120	- and osmotic resistance	310	Sulphuric acid, chemical data	104
- - solutions, specific gravity	109	Sphingomyelin, in plasma	321	- solutions, specific gravity	107
- in sweat	298	SPIERS' eosinophil test	182	Sulphuric acids, conjugated and esterified, in	
- thiosulphate, electrolytic data	118-120	Spinal fluid. See Cerebrospinal fluid		urine	290
- - solutions, specific gravity	108	Spleen, chemical composition	282	Sun, constants of	81
- in transudates	298	Splenectomy, and HOWELL-JOLLY bodies	334	Suramin, posology	397
- acid urate, formation in urine	288	Sprue, and folic acid	220	Surface area, of body. See Body surface	
- in urine	290, 299	- and vitamin B ₁₂	222	- of erythrocytes	336
Solar constants	81	Squares and square roots, table	21 sq.	Surface tension, of aqueous humour (eye)	362
- system, constants	81, 82	Squill, posology	395	- of blood	307
- time	56	Squint, latent	364, 365	- of cerebrospinal fluid	352
Solutions (aqueous) (<i>See also Electrolytes</i>)	114, 115	S.R. (sedimentation rate). See under		- of semen	276
- buffering	105	Erythrocytes		- units	63
- concentration units	76	S, s (secretor/non-secretor system)	341, 351	Susceptibility, electrical	66
- freezing-point depression and osmotic		Staff cells. See Band cells		- magnetic	68
pressure	115, 116	Staining of bacteria	129 sq.	Sweat, electrolytes	298
- ideal and real	115	Standards, biological, international	77 sq.	- water loss through	295, 296
- for infusion therapy	121 sq.	Standard clearance, renal	300	Sweets, chemical composition	238, 239
- molality and molarity	114	Standard deviation	32	Swine erysipelas serum, international standard	77
- 0.1-normal, of reagents	104	Standard man, data of	101	Symbols, for dimensions, units and constants	49
- osmolality and osmolarity	115	STANNUS's cerebellar syndrome	216	- of elements, alphabetical list	83
- osmotic concentration and pressure,		Staphylococci	130	- for multiples and submultiples	7
calculation	115, 116	- antitoxins, international standards	77	- of units, index	50
- specific gravity	107 sq.	Starvation, and blood magnesium	327	Sympathicolitics, effect on pupil	357
Somatropic hormone	192	Statistical methods	31 sq.	Sympathomimetics (adrenaline, noradrena-	
SOMMERFELD's fine-structure constant	81	- tables	25-30	line)	205
SONTAG method for skeletal age	268	Stearic acid, in breast milk	229	- effect on pupil	357
SØRENSEN's buffer solution	105	STEFAN-BOLTZMANN constant	81	Sympatol. See Phenylephrine tartrate	
Sound units	73	Sternal marrow, myelogram	340	Syndrome, ADIE's	359
Space constant, electric. See Permittivity,		Steroids	195 sq.	- adrenogenital	183
absolute		- urine, formaldehydogenic	182	- chiasmal	365
- magnetic. See Permeability, absolute		Steroid hormones. See under Hormones		- clivus border	365
Sparteine sulphate, posology	395	Sterols, in body and organs	282	- CUSHING's	183, 193
Specific charge of elementary particles	80	Stibium. See Antimony		- FOSTER-KENNEDY	365, 366
- conductivity. See Electrical conductivity		Stibophen, posology	395, 419	- LORAIN-LEVY	193
Specific gravity, of acetic acid solutions	108	Stilb	72	- MARCHIAFAVA-MICHELI	291
- of ammonia solutions	110	Stilboestrol (diethylstilboestrol), chemical		- pupillary	359
- of aqueous humour (eye)	362	data	103	- STANNUS's cerebellar	216

Note that this index does not include the Supplement (pages 427-519).

This has been separately indexed on pages 520-528.

Synonyms

Urea

The following special indexes are also available:

Symbols and abbreviations for units page 50

Names and symbols of the elements page 83

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

S	page
Synonyms of pathogenic organisms and infectious diseases	172 sq.
Syphilis, and antibiotics	149
Systems of measurement	49
Systematic classification of bacteria, protozoa and worms	169 sq.
Systolic blood pressure	302

T	page
t-distribution	38
- and probability, table	30
T (tera-, symbol for 10^{12})	7

Taeniocides. See Teniacides	
Tantalum, properties and isotopes	92
Tapeworm remedies	163
Tartar emetic (antimony potassium tartrate), chemical data	103
- posology	370
Tartaric acid, chemical data	104
Taurocholates, in bile	283
Tears, composition and properties	362
Technetium, properties and isotopes	88
Teeth, development of	271
Tellurium, properties and isotopes	90
Temperature, definition and scales	56, 57
- Centigrade-Fahrenheit conversion table	58
Teniacides	163
Tera- (symbol for 10^{12})	7
Terbium, properties and isotopes	91
Teroprotein	219
Terramycin. See Oxytetracyclin	
Test, alkali loading (renal function, acidosis)	288
- ASCHHEIM-ZONDEK (pregnancy)	179
- ascorbic acid (ACTH)	182
- BENEDICT (sugar)	294
- COOMBS (anti-human globulin)	341, 343
- cover (latent strabismus)	365
- cross-matching (blood compatibility)	343
- dilution (renal function)	288
- eosinophil (adrenocortical function)	189
- FEHLING'S (sugar)	294
- FRIEDMAN (pregnancy)	179
- gold sol (spinal fluid)	353
- MADDOX (latent strabismus)	365
- NONNE-APELT (spinal fluid)	353
- OEHLECKER'S (blood compatibility)	343
- pregnancy	179
- QUECKENSTEDT (spinal fluid)	352
- Rana pipiens (pregnancy)	179
- ROTHERA'S (acetone bodies)	294
- SAYERS' (ACTH)	182
- SCHICK. See SCHICK test	
- SPIERS' (corticosteroids)	182
- sulphosalicylic acid (proteins)	294
- THORN (adrenocortical function)	189
- VAN DEN BERGH (bilirubin)	319, 320
- VOLHARD'S (renal function)	288
Testes, chemical composition	282
Testosterone	201
- chemistry	196
- function	204
- metabolism and structure	198
- posology	397
Tetanus, antitoxin, international standard	77
- pathogen	144
- toxoid, international standard	78
Tetany, and acidosis	297
- infantile, and vitamin D	211
Tetrachlorethylene, posology	397, 419
Tetracyclins	128 sq.
Tetraethyl-lead, poisoning. See Lead	424
Tetraethyl pyrophosphate, effect on pupil	357
Thallium, poisoning	426
- properties and isotopes	93
Thebaine, posology	397
Theobromine, chemical data	103
- posology	397, 420
Theophylline, chemical data	103
- posology	398, 420
THEORELL and STENHAGEN'S buffer	105
Thermal conductivity	63
Thermal units	61
Thiamine. See Vitamin B ₁	
Thiopentone sodium, posology	398

T	page
Thiouracil, and thyroid function	208
Thorium, properties and isotopes	96
Thorium-A, -B, -C, -C'	94
Thorium-C''	93
Thorium-X	95
THORN test	189
Thousandth mass unit	61
Threadworms. See Nematodes	
D(-)-Threonine	224
- in breast milk	228
- in plasma	317
- of plasma proteins	315
- in urine	289
Thrombocytes, blood count	338
- genealogy	332
- variation during growth	333
Thromboplastin (thrombokinase), and prothrombin time	310
Thrush	168
Thulium, properties and isotopes	92
Thymol, posology	398
Thymol blue, indicator range	106
Thymolphthalein, indicator range	106
Thyroglobulin	208
Thyroid, chemical composition	282
- dried, posology	398, 420
Thyrotropic hormone (thyrotropin)	181
- international standard	78
Thyroxine	207, 208
- posology	398, 420
Time units	56
Tin, in blood	329
- in organs	282
- properties and isotopes	89
Tissue, connective. See Connective tissue	
- lymphatic, effect of ACTH/adrenocortical hormones	188
Titanium, properties and isotopes	86
Tj ^a antibody (blood group Jay)	351
TMU (thousandth mass unit)	61
Toadstools, poisoning	425
TOCANTINS' blood coagulation theory	312
Tocopherols. See Vitamin E	
Tolerance doses (radiation)	71, 99, 100
Toluene poisoning. See under Petroleum	
spirit	425
Ton (weight)	55, 56
- (register, shipping)	54
Tone frequencies	73
- intervals	74
- scales	74
Tonicity. See Osmolality	
Tonometer values for intraocular pressure	362
Torr (mm Hg)	61
Toxoplasmosis	159
TPN (triphosphopyridine nucleotide)	218
Trace elements, in blood	329, 330
- in organs	282
Trans-configuration of steroids	195
Transfusion, blood. See under Blood	
Transmethylation, and vitamin B ₁₂	221
Transpiration, invisible	295, 296
Transudates, electrolytes in	298
Transuranic elements, properties and isotopes	97
Tribromoethyl alcohol, posology	398
Trichina worm	167
Trichomonas vaginitis	159
Trigonelline, urinary excretion	218
1:3:5-Trinitrobenzene, indicator range	106
Triphosphopyridine nucleotide	218
Tromexan. See Ethyl biscoumacetate	
Tropeolin 00, indicator range	106
Tropical year	56, 81
Troposphere, abundances of elements	84 sq.
Troxidone, children's doses	420
Troy weight	51, 55
Trypaffavin, blood circulation time from	301
Trypanocides, international standards	79
Trypanosomes	158
Trypsamide, chemical data	103
- posology	398, 420
L(-)-Tryptophan	224, 225
- in breast milk	228
- and nicotinic acid synthesis	218
- in plasma	317
- of plasma proteins	315
- in urine	289

T	page
Tuberculin, old, international standard	78
- - posology	399
Tuberculins, international standard protein derivatives	78
Tuberculin test, effect of ACTH/adrenocortical hormones	188
Tuberculosis and antibiotics	145
Tuberculum sellae, meningioma of, ocular symptoms	366
Tubocurarine chloride, chemical data	103
- international standard	79
Tubular function values	300
Tumours, brain, and ocular symptoms	365, 366
Tungsten, properties and isotopes	92
Turpentine poisoning	426
TWADDELL hydrometer scale	109
Typhoid antiserum, international standard	77
- pathogen	139
Typhus fever	151
Typographical units	52
L(-)-Tyrosine	224
- in plasma	317
- of plasma proteins	315
- in urinary sediments	292, 293
- in urine	289

U	page
Ulcers, corneal, ocular symptoms	364
- gastric, effect of ACTH/adrenocortical hormones	189
- - and gastric juice	286
Undecylenic acid, chemical data	103
Units of measurement	49
- acceleration	59
- acoustic	73
- action	62
- analytical	76
- angle	57
- angular acceleration and velocity	59
- area	53
- astronomical	52, 56, 82
- biological, international	77 sq.
- British and US system	51
- chemical	75, 114
- concentration	76
- density	60
- electrical, electromagnetic, electrostatic	64 sq.
- energy	61
- entropy	62
- force	59, 60
- frequency	59
- index of	50
- length	52
- light	72
- magnetic	64 sq.
- mass	55, 56
- photometric	72
- power	62
- pressure	60
- radiation	70, 71
- sound	73
- symbols	50
- of radioactive decay	70
- temperature	56, 57
- - conversion	58
- thermal	61-63
- time	56
- typographical	52
- velocity	57
- viscosity	63
- volume	53, 54
- weight	55, 56, 59, 60
- work	61, 62
Unit skin dose	70
Unsaturated fatty acids, in blood	321
- in breast milk	229
- and vitamin F	223
Uranium, properties and isotopes	96
Uranium-X ₁ , -X ₂ , -Y, -Z	96
Uranus, planetary constants	82
Urates, in urinary sediments	292, 293
Urea, in aqueous humour (eye)	363
- in breast milk	228
- in cerebrospinal fluid	353
- chemical data	103

Urea (continued)

The following special indexes are also available:

Symbols and abbreviations for units page 50

Names and symbols of the elements page 83

Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

U	page	V	page	V	
Urea,		Veriazol, children's doses	421	Volume,	
- children's doses	420	Vermes. See Worms		- of intestinal juice	2
- in gastric juice	284	Veronal poisoning. See under Barbiturates	423	- of intracellular space	
- in lacrimal secretion	362	Vibrio, cholera	129	- of lacrimal secretion	
- nitrogen, conversion factors	126	L-5-Vinyl-2-thio-oxazolidone	208	- of lens (eye)	
- in pancreatic juice	283	Virales	153 sq.	- of pancreatic juice	2
- in plasma	317	Virilism, in adrenogenital syndrome	183, 201	- per cent (vol%)	
- and protein intake	317	Viruses	153 sq.	- of renal water loss	288, 295, 2
- renal clearance	300	Viscosity, of aqueous humour (eye)	362	- of saliva	2
- in saliva	283	- of blood	306	- of sweat	
- in semen	277	- of cerebrospinal fluid	352	- units	
- in urine	288	- of semen	276	- of urine	288, 295, 2
Ureides, poisoning. See under Barbiturates	423	- units	63	- of vitreous (eye)	
Urethane, chemical data	103	- of vitreous (eye)	364		
- posology	399, 420	Vision, scotopic, photometric units for	72	W	
Uric acid, in aqueous humour (eye)	363	Vision-testing charts	(inside back cover)	W (watt)	
- in breast milk	228	Visual acuity, test charts	(inside back cover)	WARBURG's respiratory enzyme	
- in foods	231 sq.	Visual fields	361	Water, daily intake and elimination	2
- in gastric juice	284	- defects	360, 361	- daily requirement	
- nitrogen, conversion factors	126	- pathways	360	- distribution in body	
- in pancreatic juice	283	- purple. See Rhodopsin		Water balance	101, 2
- in plasma	318	Vital capacity	251 sq.	- in pregnancy	
- in saliva	283	- of children	254	Water column, pressure of 1 mm	
- in urinary sediments	292, 293	- of men	252	Water content, of bile	
- in urine	288	- of women	253	- of body	28
Urine	288 sq.	Vital-staining erythrocytes. See Reticulocytes		- in pregnancy	
- acetone bodies	289	Vitamins, in breast milk and colostrum	228, 229	- of faeces	
- amino-acids	289	- in cow's milk	228, 229	- of foods	2
- colour	291	- daily requirements	226	- of intestinal juice	
- electrolytes	290, 299	- fat-soluble	209 sq.	- of organs	
- hormones	290	- in foods	230 sq.	- of pancreatic juice	
- pH value	288	- posology	399, 421	- of saliva	
- excretion of minerals in faeces and	287	- international standards	78	- of serum	11
- physical properties	288	- water-soluble	213 sq.	Water and electrolyte balance	2
- porphyrins	291	Vitamin A	209	Water loss, of body	29
- proteins	288	- posology	399, 421	Water metabolism, effect of ACTH/adrenal	
- and renal function	299, 300	Vitamin B ₁	214	- corticoid hormones	
- sediments	292, 293	- and blood pyruvic acid	322	- effect of posterior pituitary hormones	
- steroid hormones	196, 200 sq.	- posology	370, 421	Water-soluble vitamins	2
- sugars	289	- international standard	78	Watt	
- tests	294	Vitamin B ₂ (riboflavin)	215	Wb (weber)	
- urea	288	- posology	393, 421	WBC (white blood count). See under Leuco	
- vitamins	290	Vitamin B ₆	217	- cytes	
- volume	288	Vitamin B ₁₂	221	Weber	
Urobilin, in urine	291	- in carbon tetrachloride poisoning	211	WEBER-FECHNER law	
Urobilinogen, in faeces	287	- posology	377	Weight, body. See Body weight	
- in urine	291	Vitamin Bc	219	- distribution in standard man	
Uroporphyrins, in urine	291	Vitamin C (ascorbic acid)	213	- of organs	
Urotropine. See Hexamine		- and adrenaline in adrenal medulla	203	- units	55, 56,
U.S. PHARMACOPEIA, usual doses	367 sq.	- in aqueous humour and lens (eye)	365	WESTERGREEN blood sedimentation methods	
Usual doses	367 sq.	- intake and blood level	324	Whey, amino-acid composition	
Uterus, changes during pregnancy and		- in prostate secretion	278	Whipworm	
- puerperium	274	- posology	371, 421	White blood cells. See Leucocytes	
- chemical composition	282	- international standard	78	White hypertension	
- effect of oxytocin	194	Vitamin D	210	White mouth	
		- poisoning	211	Whooping cough	
		- posology	373, 421	WIEN's displacement constant	
V		Vitamin D ₂ . See Calciferol		WOHLGEMUTH's diastase unit	
val (gram equivalent)	75	Vitamin D ₃ , children's doses	421	Women (See also Menstrual cycle,	
Vacuum, impedance of	80	- international standard	78	- Pregnancy, etc.)	
- velocity of light in	80	Vitamin E	211	- basal metabolism	2
Vaginal secretion, pH value	276	- international standard	78	- blood pressure	
Vaginitis, Trichomonas	159	Vitamin F	223	- blood sedimentation	
Valency of elements	84 sq.	- in blood	321	- body water	
Valerian, children's doses	421	- in breast and cow's milk	228	- gonadotropin excretion	
L(+)-Valine	224	Vitamin H (biotin)	218	- height and weight	
- in breast milk	228	Vitamin K (menadione)	212	- nutritional requirements	
- in plasma	317	- posology	384, 421	- obstetric norms	
- of plasma proteins	315	- daily requirement	227	- vital capacity	
- in urine	289	Vitamin P (citric)	214	Work units	
Vanadium, properties and isotopes	86	Vitrein, in vitreous (eye)	364	Worms	1
VAN DEN BERGH reaction of blood	319, 320	Vitreous humour (eye)	364	- index of diseases and	1
Variance, statistical	32	Vol% (volume per cent)	76	- classification	
Variola	153	Volatile oils, poisoning	426		
Vasopressin	194	VOLHARD's test for renal function	288	X	
- injection, posology	399	Volt	64	χ ² -distribution, calculation with	
Vegetables, chemical composition	232 sq.	Volume, of aqueous humour (eye)	362	- table of probabilities	
Velocity units	57	- of bile	283	Xanthine oxidase	
Venous blood. See under Blood		- of blood and plasma	295, 305	Xanthochromia of cerebrospinal fluid	
Ventricle, right, blood pressure in	302	- of ejaculate	276	Xanthocyanopsia (test chart inside back cover)	
Ventricles, brain, tumours of, ocular symp-		- of extrarenal water loss	295, 296	Xanthopterin, Xanthopterin aldehyde	
- toms	366	- of extracellular space	295	Xenon, properties and isotopes	
Ventricular fluid (See also under Cerebrospinal		- of eyeball	356	Xerophthalmia, and vitamin A	
- fluid), sugar content	354	- of faeces	287, 295, 296		
Venus, planetary constants	82	- gas, correction to normal	127		
Verdohaemoglobin, in blood	338	- of gastric juice	284 sq., 296		
		- of interstitial space	295		

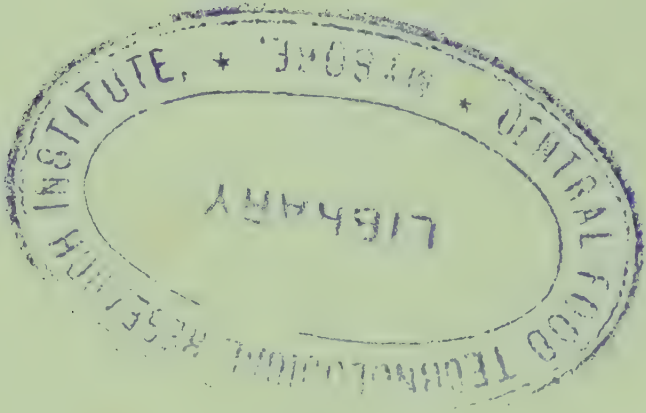
Note that this index does not include the Supplement (pages 427-519).
This has been separately indexed on pages 520-528.

Zoopherin

The following special indexes are also available:

Symbols and abbreviations for units page 50
Names and symbols of the elements page 83
Pathogenic organisms (bacteria, protozoa, worms) and infectious diseases pages 172-178

	page	Y	page	Y	page
-rays, biological activity	71	Yeast,		Yttrium, properties and isotopes	88
scattering constants	81	- chemical composition	242		
units	70	- in gastric juice	286	Z	
-ray spectroscopic unit	52	- <i>meso</i> inositol in	223	Z (atomic number)	84 sq.
-unit, SIEGBAHN'S	52	- nicotinic acid in	217, 242	Zinc, in blood	330
ylene poisoning. See Petroleum spirit . . .	425	- pantothenic acid in	216	- in lens (eye)	363
		- para-aminobenzoic acid in	219	- properties and isotopes	87
		- vitamin B ₁ in	214, 242	- in vitreous (eye)	364
		- vitamin B ₂ in	215, 242	- sulphate, chemical data	104
		- vitamin B ₆ in	217	- - posology	399
aws	149	Yellow fever	155	Zirconium, properties and isotopes	88
ear, sidereal and tropical	56, 81	Yohimbine, posology	399	Zoopherin	221
east, biotin in	218	YOUNG's rule for dosage	401		
		Ytterbium, properties and isotopes	92		



Due Date Return Date Due Date

Call No. Ae N59

To be issued from :

<i>Due Date</i>	<i>Return Date</i>	<i>Due Date</i>	<i>Return Date</i>

REFERENCE 4396

Acc. No.

N59

LE

entax

leg

